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CONTENTS OF VOLUME 3

JULY, 1921. NUMBER 1

| | |
|--|-----|
| THE ANATOMY AND SURGERY OF THE TRIGON. HUGH H. YOUNG, M.D., AND MILEY B. WESSON, M.D., BALTIMORE..... | 1 |
| DIVERTICULA OF THE URINARY BLADDER. W. E. LOWER, M.D., CLEVELAND | 38 |
| TUMORS OF THE BONY CHEST WALL. C. A. HEDBLUM, M.D., ROCHESTER, MINN. | 56 |
| A STUDY OF RESECTION OF THE PYLORUS FOR GASTRIC ULCER: REPORT OF CASE. KARL W. DOEGE, M.D., MARSHFIELD, WIS..... | 86 |
| TRAUMATIC SPONDYLOLISTHESIS: REPORT OF TWO CASES. S. KLEIN- BERG, M.D., NEW YORK..... | 102 |
| STUDIES IN EXHAUSTION. II. EXERTION. G. W. CRILE, M.D., CLEVELAND | 116 |
| THE COURSE OF RECOVERY FOLLOWING TRAUMA OF THE SPINAL CORD. STANLEY COBB, M.D., BOSTON, AND C. C. COLEMAN, M.D., RICHMOND, VA. | 132 |
| FRACTURE OF THE SKULL: IMPORTANCE OF THE EARLY DIAGNOSIS AND OPERATIVE TREATMENT OF FRACTURE OF THE SKULL, WITH CHART OF CLINICAL CLASSIFICATION AND TREATMENT, AND GUIDE FOR DETAILED NEUROLOGIC EXAMINATION. WELLS P. EAGLETON, M.D., NEWARK, N. J. | 140 |
| CHOLECYSTITIS: ETIOLOGY, DIAGNOSIS AND TREATMENT. ROSCOE R. GRAHAM, M.B. (TOR.), TORONTO, CANADA..... | 154 |
| FURTHER OBSERVATIONS ON THE CLINICAL VALUE OF CERTAIN BACTERIO- STATIC TRIPHENYLMETHANE DERIVATIVES. C. COLEMAN BERWICK, A.M., SAN FRANCISCO..... | 168 |
| FIFTEENTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY. ROBERT B. OSGOOD, M.D.; ROBERT SOUTTER, M.D.; HARRY C. LOW, M.D.; MURRAY S. DANFORTH, M.D.; C. HERMANN BUCHOLZ, M.D.; LLOYD T. BROWN, M.D., AND PHILIP D. WILSON, M.D., BOSTON..... | 181 |
| EDITORIAL REVIEW: CONGENITAL CLEFT OF THE LIP AND PALATE. HARRY P. RITCHIE, M.D., ST. PAUL..... | 230 |

SEPTEMBER, 1921. NUMBER 2

| | |
|---|-----|
| PERFORATING HEMORRHAGIC (CHOCOLATE) CYSTS OF THE OVARY: THEIR IMPORTANCE AND ESPECIALLY THEIR RELATION TO PELVIC ADENOMAS OF ENDOMETRIAL TYPE ("ADENOMYOMA" OF THE UTERUS, RECTO- VAGINAL SEPTUM, SIGMOID, ETC.). JOHN A. SAMPSON, M.D., ALBANY, N. Y. | 245 |
| IS PAGET'S DISEASE OF THE NIPPLE PRIMARY OR SECONDARY TO CANCER OF THE UNDERLYING BREAST? ALSON R. KILGORE, M.D., SAN FRANCISCO | 324 |
| SQUAMOUS-CELL CARCINOMA OF THE URINARY BLADDER. ALBERT J. SCHOLL, JR., M.D., ROCHESTER, MINN..... | 336 |
| CANCER OF THE BREAST. BYRON B. DAVIS, M.D., OMAHA..... | 348 |

CONTENTS OF VOLUME 3

SEPTEMBER, 1921—Continued

| | |
|--|-----|
| OBSERVATIONS BASED ON A STUDY OF INJURIES TO THE ELBOW. ISIDORE COHN, M.D., NEW ORLEANS..... | 357 |
| TORSION OF THE CECUM AND ASCENDING COLON. JOHN HOMANS, M.D., BOSTON | 395 |
| BLOOD NITROGEN ESTIMATIONS IN GENITO-URINARY AND ABDOMINAL CONDITIONS. J. W. VAUGHAN, M.D., AND P. F. MORSE, M.D., DETROIT | 405 |
| FUNCTION IN RELATION TO TRANSPLANTATION OF BONE. S. L. HAAS, M.D., SAN FRANCISCO..... | 425 |
| THE COMPOSITION OF APPENDICEAL CONCRETIONS. MARY E. MAVER AND H. GIDEON WELLS, CHICAGO..... | 439 |

NOVEMBER, 1921. NUMBER 3

| | |
|---|-----|
| THE PATHOLOGY OF CHRONIC CYSTIC MASTITIS OF THE FEMALE BREAST: WITH SPECIAL CONSIDERATION OF THE BLUE-DOMED CYST. JOSEPH COLT BLOODGOOD, M.D., BALTIMORE..... | 445 |
| THE ACHIEVEMENTS AND LIMITATIONS OF NEUROLOGIC SURGERY. CHARLES H. FRAZIER, M.D., PHILADELPHIA..... | 543 |
| A REVIEW OF A YEAR'S SERIES OF INTRACRANIAL TUMORS: JUNE, 1920, TO JUNE, 1921. CHARLES EDWARD LOCKE, JR., M.D., BOSTON..... | 560 |
| POSTOPERATIVE BILIARY FISTULAS. DONALD C. BALFOUR, M.D., AND JAMES W. ROSS, M.B. (TOR.), ROCHESTER, MINN..... | 582 |
| THE SUSPENSION TRACTION TREATMENT OF FRACTURES OF THE LONG BONES NEAR LARGE JOINTS. JOHN A. HARTWELL, M.D., NEW YORK | 595 |
| THE RELATION OF SURGICAL TECHNIC TO GASTROJEJUNAL ULCER. ROEDER, M.D., OMAHA..... | 622 |
| A METHOD OF DETERMINING THE EARLY REGENERATION OF NERVE FIBERS AT OPERATION. JULIAN Y. MALONE, M.D., ST. LOUIS..... | 634 |
| INTESTINAL OBSTRUCTION. DONALD K. BACON, M.D.; ROBERT E. ANSLOW, M.D., AND HAZEL H. EPPLER, DETROIT..... | 641 |

ARCHIVES OF SURGERY

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JULY, 1921

No. 1

THE ANATOMY AND SURGERY OF THE TRIGON *

HUGH H. YOUNG, M.D. AND MILEY B. WESSON, M.D.

BALTIMORE

The trigonal muscle is of particular interest in a study of the mechanism of micturition, because of its peculiar anatomy and close relationship with the so-called vesical sphincters. The opening of the internal "sphincter" during micturition was formerly considered as an inhibitory action. We now believe that the contraction of the powerful trigonal muscle passing in the form of a bow through the weaker arcuate muscles at the vesical orifice helps mechanically to pull open the "sphincter." This view is confirmed by endoscopic and cystoscopic studies, as the trigonal muscle is seen to contract and pull open the vesical orifice.

Obstruction to urination is generally followed by a partial or complete compensatory hypertrophy of the trigon. Upon removal of the obstruction, there is a corresponding compensatory trigonal atrophy. Occasionally following marked obstruction there is an undermining of the trigon, the hypertrophied muscle being dissected away from the bladder wall. Upon contraction it stands up as a ledge dividing the bladder into two parts, mechanically preventing the complete emptying of the bladder. Furthermore, the contractile force of such a trigon is not properly applied to expedite the opening of the vesical orifice. With the removal of the obstruction by splitting the damlike ledge, the trigon is able to resume its normal functions. However, if there has been a complete removal of the trigon, micturition is not normal in that the bladder is not completely emptied.

MORPHOLOGY

The trigon (tr. Lieutaudii) is a smooth triangular area lying in the base of the bladder, having the two ureters and the vesical orifice at its angles. It is better to conceive of the trigon as a region rather than to assign this name to any structure or structures. In the trigonal region are the two muscle layers of the bladder wall, the external longitudinal and the internal circular, and superimposed upon these is the sub-

*From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital.

mucous or trigonal muscle, which is an extension of the longitudinal muscle layer of the ureters and their sheaths.¹ It consists of fibers extending fanwise from the ureteral orifices, some fibers passing medially, going to make up Mercier's bar, others interlacing with corresponding fibers from the opposite side in the middle of the trigon, and still others passing down to the urethra and making up Bell's² muscles. The Bell's muscles of the two sides converge at the vesical orifice, causing the trigonal muscle at this point to be denser and thicker.³ Where the thickened layer passes over the edge of the vesical orifice, it makes up the principal portion of the uvula of Lieutaud.

The mucous membrane of the trigon differs from that of the remainder of the bladder in that it is so firmly adherent to the subjacent tissue as to present rarely any rugae even when the bladder is empty, thus preventing any prolapse of the mucous membrane into the vesical orifice during micturition.⁴ Subtrigonal glands occur commonly in the anterior half of the trigon, lying between the vesical orifice and the middle of the trigon.⁵ They are generally simple tubules lying in the mucosa though they may have one or two small branches, and extend superficially into the muscle layer. They do not have definite connective tissue or other differentiated envelopes surrounding them. In our series we saw three hypertrophies of this group, the tumor masses appearing to be about 1 cm. in diameter and 0.5 cm. in height. They are of little clinical importance (Fig. 1).

The observation made of the gross specimens studied show that no rules can be deduced as to shape⁶ and size⁷ of the trigon, as it displays

1. Satani, Y.: Histologic Study of the Ureter, *J. Urol.* **4**:247, 1919.
Waldeyer, W.: *Das Trigonum vesicae*, Sitzungsber. d. k. Akad. d. Wissensch. Math.-naturw. Cl., 1897, p. 732.

2. Bell, C.: Account of the Muscles of the Ureters and Their Effects on the Irritable State of the Bladder, *Med.-Chir. Tr.* **3**:171-190, 1812.

3. Ellis, G. V.: An Account of the Arrangement of the Muscular Substance in the Urinary and Certain of the Generative Organs of the Human Body, *Med.-Chir. Tr.* **39**:327-338, 1856.

4. Treves, F.: *Surgical Applied Anatomy*, Ed. 7, London, Cassell & Co., 1918, p. 475.

5. Lowsley, O. S.: The Gross Anatomy of the Human Prostate Gland and Contiguous Structures, *Surg., Gynec. & Obst.* **20**:183-192, 1915; The Development of the Human Prostate Gland with Reference to the Development of Other Structures at the Neck of the Urinary Bladder, *Am. J. Anat.* **13**:299-346, 1912.

6. Disse, J.: Die Harnblase, in *Handb. d. Anat. d. Mensch.* Jena, Bardeleben **7**: Pt. 1, 113-169, 1902. Testut, L.: Vessie, in *Traité d'anatomie humaine*, Paris **3**:869-895, 1894.

7. Schewkunenko, W. N.: Portion intraparietale de l'uretere et trigone vesical, leurs differentes formes, *J. d'urol. méd. et chir.* **1**:131, 1912.

great individual variations, independent of age, sex or size of the bladder.⁸ The size of the ureteral orifices and the topography in relation to the interureteral ridge vary greatly; but both ureteral openings are never on the same side of the median line.⁹ When there are supernumerary ureters opening into the bladder, the meatus of each as a rule lies in the trigon.¹⁰ Delbet¹¹ states that in congenital absence of the ureter the corresponding side of the trigon is lacking.

MUSCULATURE OF THE VESICAL NECK

The development of the trigon was studied by one of us,¹² using a series of thirty human embryos from the Carnegie Institute of Embryology. This work was supplemented by a study of serial sections



Fig. 1.—Hypertrophy of subtrigonal gland (B. U. I., No. 2,129).

of trigons from adults. Glass models were made of the neck of the bladder of a 7½ months' fetus, cut sagittally, and of a term fetus, cut transversely. Preparations of the gross trigon were made by floating

8. Krasa, F. C., and Paschkis, R.: *Das Trigonum vesical der Säugetiere*, *Ztschr. f. urol. Chir.* **6**:1-52, 1921. Whiteside, G. S.: *The Measurements of the Trigon*, *Med. Sentinel* **12**:553-560, 1904.

9. Uteau, R.: *Anatomie du trigone vesical*, *Ann. d. mal. d. org. génito-urin.* **23**:241-290, 1905.

10. Mertz, H. O.: *A Review of the Subject of Multiple Ureters with a Study of Sixteen Unpublished Cases*, *Urol. & Cutan. Rev.* **22**:553-565, 1918.

11. Delbet, P.: *Vessie*, in *Traité d'anatomie humaine*, Paris, Poirier and Charpy **5**:74-126, 1901.

12. Wesson, M. B.: *Anatomical, Embryological and Physiological Studies of the Trigon and Neck of the Bladder*, *J. Urol.* **4**:279-315 (June) 1920.

the trigonal muscle off the bladder wall by Mall's¹³ acetic acid method (Fig. 2). The arrangement of the muscles of the so-called internal sphincter was verified by a study of specimens macerated in hydrochloric acid and teased out with needles.

The bladder has an internal circular and an external longitudinal layer of smooth muscle, which are not perfectly defined. Confusion is increased by the fact, to which Howell¹⁴ calls attention, that the direction of these fibers and the number of layers into which they can be separated depend to a large extent on the state of distention of the bladder, as the muscle fibers rearrange themselves during changes in the size of the bladder. In the trigonal region, there is in addition the trigonal muscle which embryologically is of mesodermal origin, while the external longitudinal and internal circular layers arise from tissues of entodermal origin.¹⁵

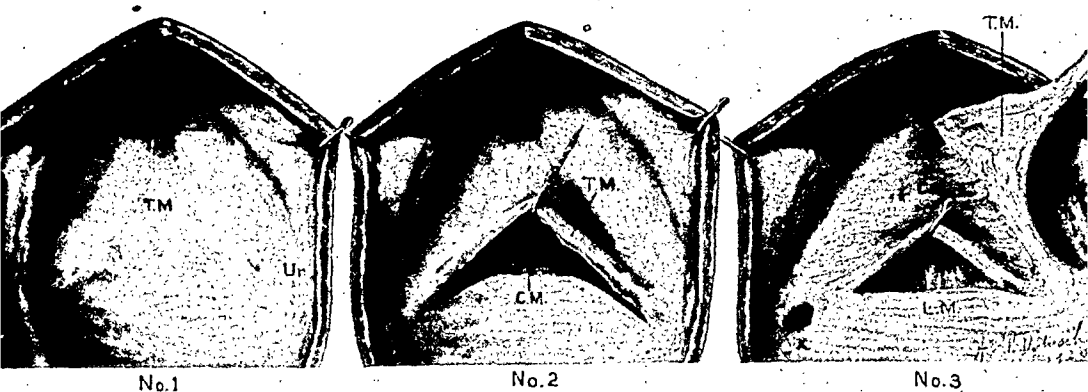


Fig. 2.—1, normal trigon; 2, trigonal muscle raised exposing the circular muscle layer; 3, left ureter dissected free from the bladder wall and trigonal muscle pulled up as a sheet. The line of cleavage is marked by a layer of blood vessels. The external longitudinal layer of muscle is exposed by lifting the circular layer: *V*, vesical orifice; *U*, ureter; *Ur*, ureteral orifice; *TM*, trigonal muscle; *CM*, circular muscle; *LM*, longitudinal muscle; *X*, opening from which ureter was removed.

In considering the muscular mechanism, making up what has been called the internal sphincter of the bladder, the reader is referred to Figure 3 and the accompanying diagram (Fig. 4) made from the glass models.

13. Mall, F. P.: Reticulated Tissue and Its Relation to the Connective Tissue Fibrils, Johns Hopkins Hosp. Rep. 1:171-208, 1896.

14. Howell, W. H.: A Text-Book of Physiology, Ed. 7, Philadelphia, 1918, W. B. Saunders Company, p. 863.

15. Felix, W.: The Development of the Urogenital Organs, in Manual of Human Embryology, Philadelphia, Keibel and Mall 2:752-979, 1912.

The fibers of the external longitudinal layer sweep down along the posterior surface of the bladder until they reach the region of the vesical orifice where many of them end. The elastic fibers continue and form a sort of tendinous arrangement connecting with the denser layers about the vesical orifice. A portion, however, of those fibers which sweep along the back of the bladder diverge slightly to form muscular bands which pass forward and downward on either side of the vesical orifice (Fig. 5). At the upper level of the urethra these two bands swing

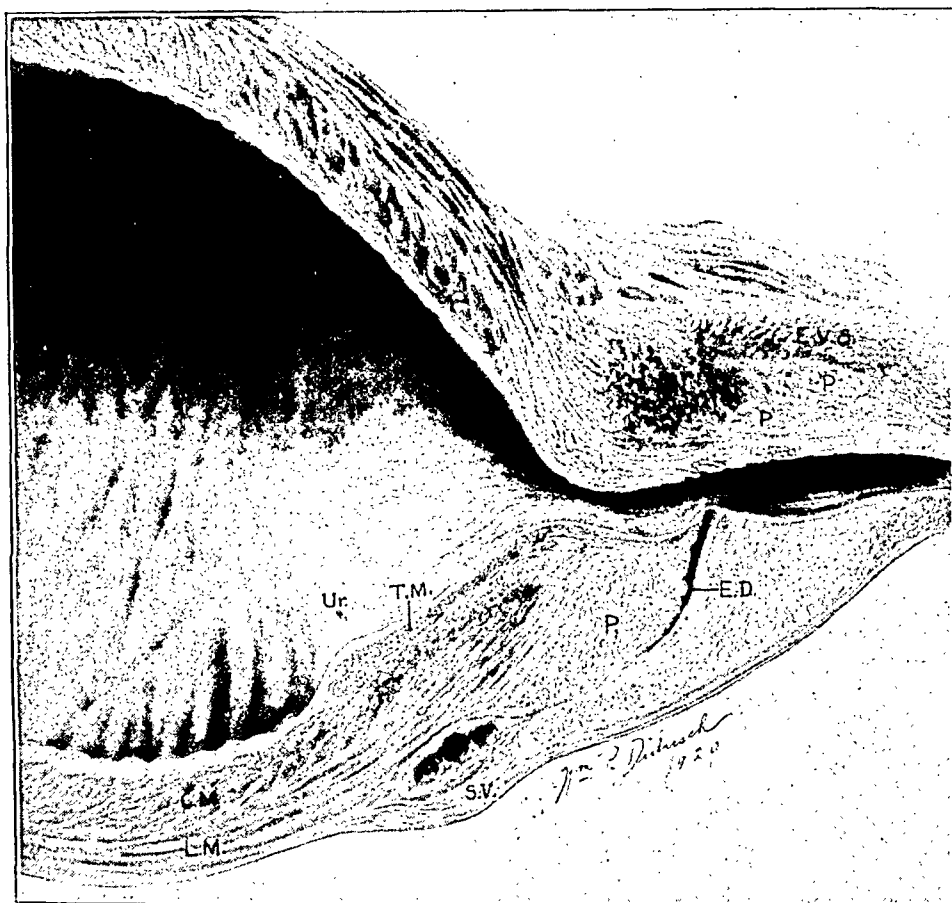


Fig. 3.—Sagittal section through urethra of adult.

medially and unite to form a loop or arch about the urethra. The fibers pass freely through this loop, and there is no raphé formation. A cross-section of this loop, where it passes in front of the urethra, is shown in the diagram (Fig. 4). The longitudinal fibers sweeping down the anterior surface of the bladder end for the most part at the vesical orifice; but a few pass along the anterior aspect of the prostatic urethra just beneath the mucosa, forming an internal longitudinal layer of the urethra, corresponding to the trigonal fibers on the posterior aspect.

The circular fibers pass around the bladder until a point is reached just opposite the vesical neck. Here some of the fibers from the region posterior to the vesical orifice swing downward and forward in an oblique direction, passing as thin bands inside the loop of the external longitudinal muscle described above and swinging around the urethra in the region generally opposite the verumontanum where they also form a loop or arch in front of the urethra. This arrangement leaves

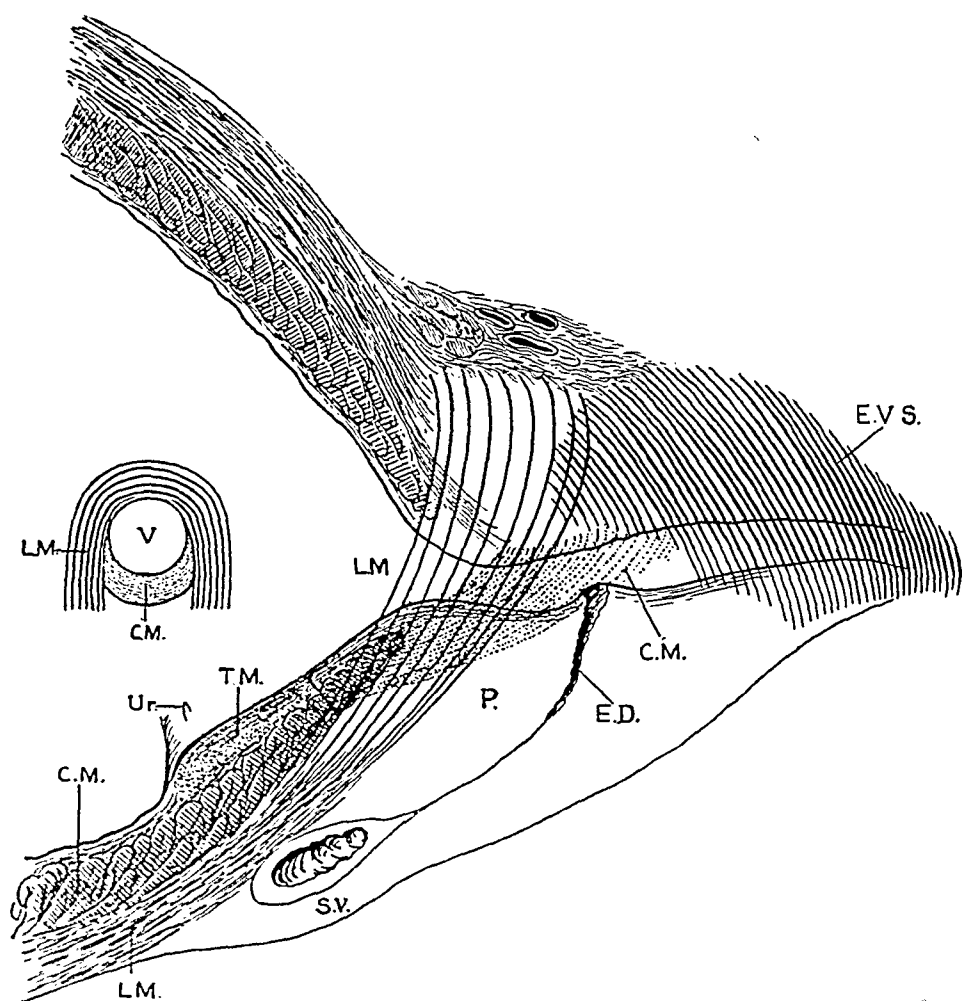


Fig. 4.—Sagittal section of bladder (diagram of Figure 3). The external longitudinal layer of the base sweeps up over the vesical orifice making a loop. Within this loop the circular layer forms a wedge below the orifice and flows down the urethra in an oblique direction surrounding the canal as a thin layer. The result is a double loop and not a sphincter. The small inset is a cross-section of the vesical orifice, showing the upward pull of the loop from the circular muscle and the opposing action of the longitudinal muscle loop. *V*, vesical orifice; *LM*, longitudinal muscle; *CM*, circular muscle; *TM*, trigonal muscle; *E.V.S.*, external vesical sphincter (striated muscle); *Ur*, ureteral orifice; *S.V.*, seminal vesicle; *E.D.*, ejaculatory duct; *P*, prostate.

a short length of the urethra extending anteriorly from the vesical orifice about half way down to the verumontanum, without any investment of fibers arising from the internal circular layer (Fig. 6). Other fibers, branching off from this band as it passes downward and forward in its oblique course, extend into the prostate gland. Their course cannot be followed among the prostatic tubules. It seems probable, however, that the prostate represents the posterior portion of this collection of circular fibers extending down around the urethra, which has been invaded and distorted by prostatic tubules.

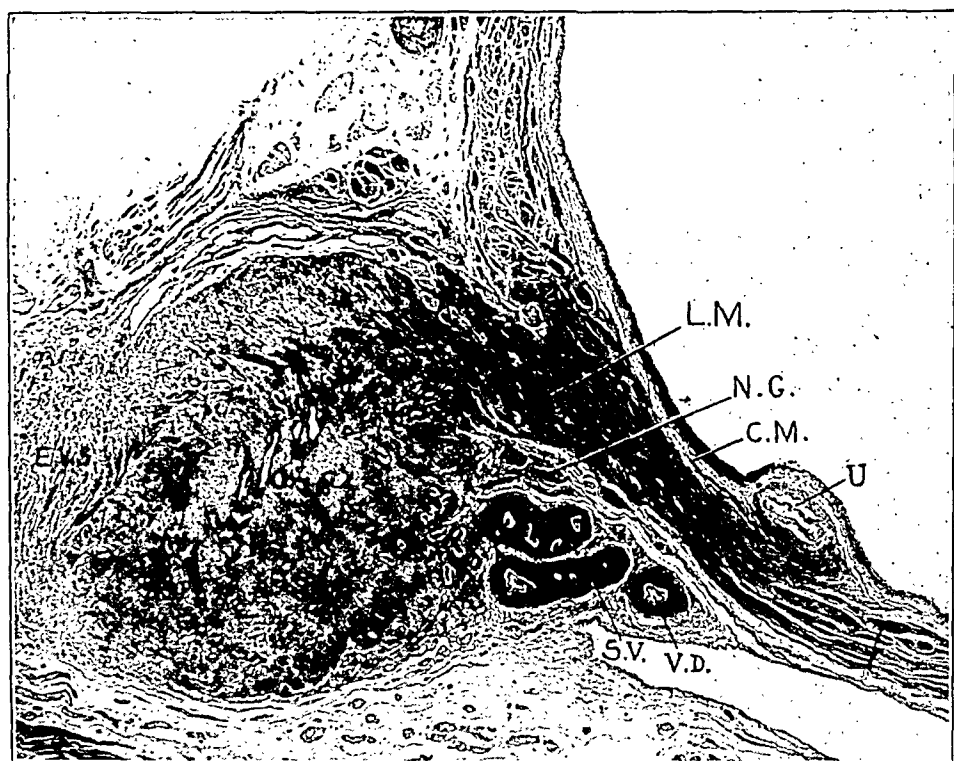


Fig. 5.—A sagittal section through lateral lobe of prostate of 240 mm. human embryo. The longitudinal layer of the base is sweeping out over the urethra making a crus over the orifice: *U*, ureter; *SV*, seminal vesicle; *VD*, vas deferens; *P*, prostate; *EVS*, external vesical sphincter; *LM*, longitudinal muscle; *CM*, circular muscle; *NG*, nerve ganglia (Embryo, Carnegie Institute 2671b, slide 46, row 2, sec. 1); $\times 9$.

The trigonal muscle, as has been described above, passes down over the posterior border of the vesical orifice and spreads out as an internal longitudinal layer over the posterior aspect of the urethra. The fibers pass between the openings of the prostatic ducts, ejaculatory ducts and prostatic utricle, and continue on down for some distance past the verumontanum. Some fibers may be traced as far as the beginning of the membranous urethra.

At a point opposite the mediolateral aspect of the vesical orifice, there may be found lying in close relationship to the fibers of the loop of the external longitudinal muscle, a few striated muscle fibers. These fibers are often quite close to the urethral mucosa and even lie between the prostatic tubules. As they pass downward and forward, they

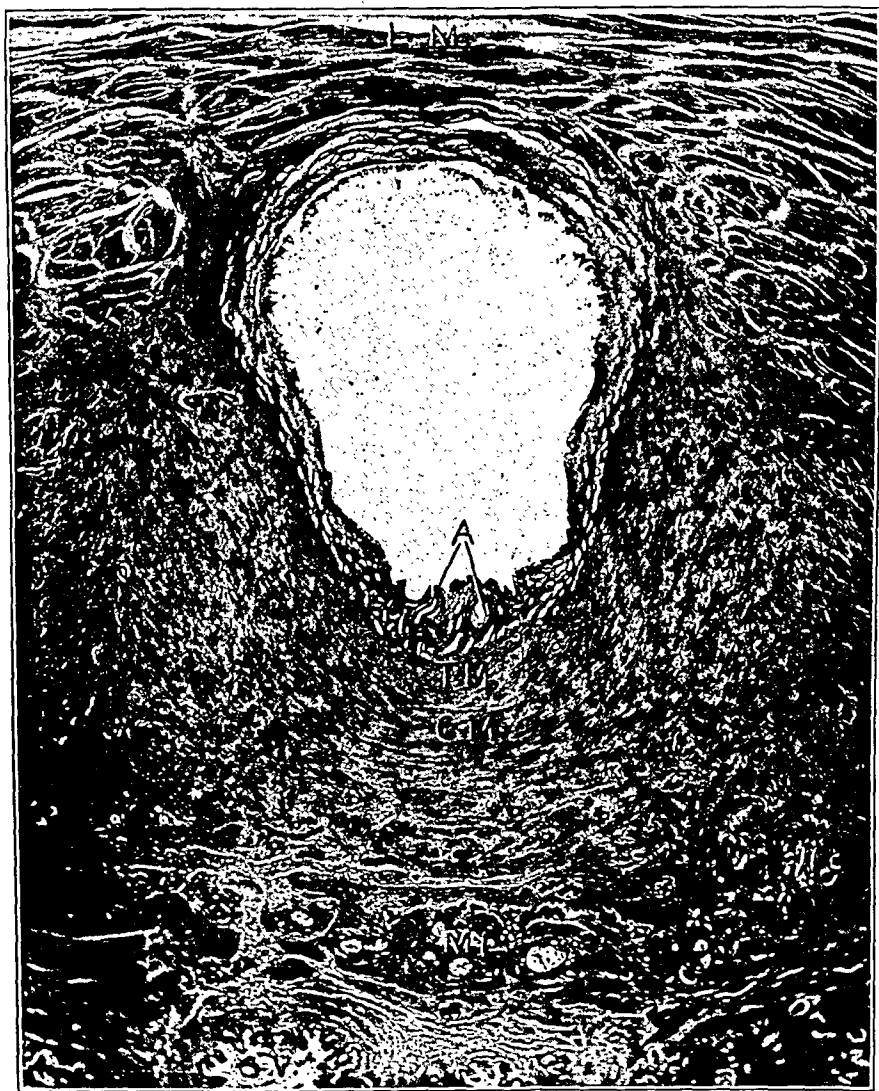


Fig. 6.—Cross-section through distal part of vesical orifice of a term human fetus. The circular layer of muscle (internal arcuate muscle) hugs the urethra but reaches only to the midlateral wall. Tubules of Albarran's glands are seen extending down through the mucosa almost to the submucous trigonal muscle. Above the urethra is the external longitudinal layer (external arcuate muscle): *LM*, external arcuate muscle; *CM*, internal arcuate muscle; *TM*, trigonal muscle; *A*, Albarran's gland tubules; *ML*, middle lobe of prostate; *LL*, lateral lobe of prostate; *SV*, seminal vesicle (Embryo, Carnegie Institute 2679, slide 2, section 2); $\times 15$.

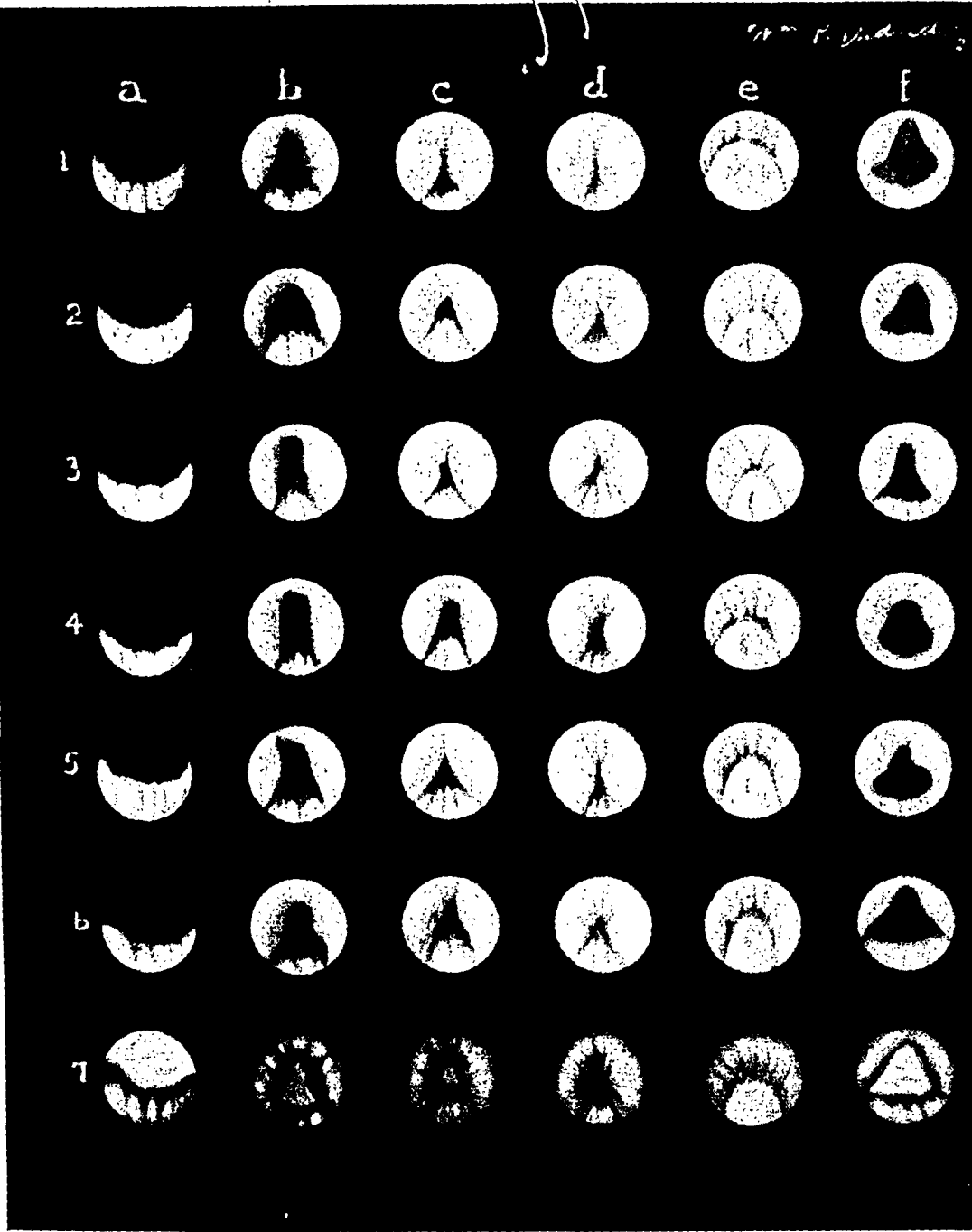


Fig. 7.—Endoscopic views of the vesical orifice and posterior urethra of six non cases. The last case was studied with a water endoscope (row 6) and also with an endoscope (row 7), for comparison of color and outline. In all other cases the water endoscope was used. In the studies the endoscope was gradually withdrawn until the verumontanum appeared; then the barrel was pushed inward until the verumontanum was just out of the field, as shown in column D. The patient then attempted to void and the contraction of the trigonal muscle pulled open the vesical orifice giving the view shown in column F.

increase in number until at a point below the lower border of the loop from the internal circular layer where it passes in front of the urethra, they pass across the midline and form a sheath of striated fibers running in a direction generally circular with regard to the urethra, but extending only about half way around it. As one passes downward, however, the fibers pass farther and farther dorsally until at a point opposite the apex of the prostate, they join those from the other side in a raphé, thus forming from this point downward a complete circular sheath about the urethra. This system of striated muscle makes up the external vesical sphincter.

It is clear that at the vesical orifice we are not dealing with a simple sphincter; i. e., a muscle whose origin and insertion is in itself. The muscle fibers comprising the pear-shaped loops about the upper end of the urethra arise from and are closely connected with the longitudinal coat of the bladder, but we do not know whether they contract in unison with it or not. The trigonal muscle exerts its pull in the direction of the open part of this muscular loop, and it undoubtedly acts to pull open or elongate the vesical orifice. The internal sphincter is a surgical designation and not an anatomic entity, the vesical orifice being closed by two loops or arcs, one arising from the internal circular layer, the internal arcuate muscle of the vesical orifice (*musculus arcuatus internus orificiae vesicalis*), and the other from the external longitudinal layer of the bladder wall, the external arcuate muscle of the vesical orifice (*musculus arcuatus externus orificiae vesicalis*).¹²

PHYSIOLOGY OF THE TRIGON

A pharmacologic study of the trigon muscle showed that it was innervated by true sympathetic fibers as it contracted on treatment with epinephrin and ergotoxin. No parasympathetic nerve endings were present as there was no response to pilocarpin, physostigmin or atropin. The bladder muscle proper gave reactions to both sympathetic and parasympathetic nerves. The tests with nicotin on the trigonal muscle gave a response indicating the presence of ganglionic structures.

Since pharmacologic and embryologic studies show an origin and nervous control different from those for the rest of the bladder, it is quite reasonable to suppose that its contraction and relaxation occur independently of those of the rest of the bladder.

A cystoscopic study of the mechanism of urination was made on a large series of patients. With the cystoscope in position, the bladder was filled to capacity with water and the patient alternately urged to strain (as for voiding urine) and then to relax. While the patient is straining, a cystoscope can be drawn down into the posterior urethra just as in a tabetic bladder. The vesical orifice, when dilated while

making an attempt to void, is not circular but is pear-shaped. This shape is undoubtedly due to the contraction of the trigonal muscle and the synchronous relaxation of the two loops of muscle about the orifice. The movement is slight and slow on the ventral aspect as the orifice dilates, but on the dorsal side the trigonal muscle accelerates and augments the relaxation of the small loop. The contraction of the trigonal muscle is powerful as shown by the depression of the floor of the urethral orifice and the marked upward movement of the verumontanum. The striae anterior to the verumontanum are apparently fixed at the lower ends, but the verumontanum moves upward with straining, and in some cases appears as if a little greater effort would cause it to enter the bladder proper. The plica ureterica remains approximately fixed throughout.

The part played by the trigon in the opening of the vesical orifice was then studied from the inside of the bladder. Cases of suprapubic cystotomies were used. The cystoscope was passed through the small fistula and the bladder filled with water. Then as the patient strained, the trigon was seen to contract as previously described, the vesical orifice opened, and normal voiding followed.

Through an endoscope the opening and closing of the vesical orifice were studied from the urethral side (Fig. 7). The instrument was passed into the bladder and was slowly withdrawn. The dorsal lip of the vesical orifice appeared first as a semicircle and then as an isosceles triangle with collapsing sides. Just before closure was complete, the patient attempted to void and there was a sluggish lateral movement outward of the sides and a quick downward pull of the base or trigonal muscle. The endoscope was then slowly withdrawn and the sides of the triangle collapsed, giving the appearance of an inverted letter "Y". This is doubtless due to the action of the trigonal muscle and of the oblique arcuate muscle of the internal "sphincter" previously described.

CHANGES IN THE TRIGON, SECONDARY TO RENAL TUBERCULOSIS, AND THE SURGICAL TREATMENT

Some of the pathologic changes that take place about the trigonal end of the ureter in cases of renal tuberculosis have been reported by one of us,¹⁶ the salient points of which will be reiterated here.

In cases of renal tuberculosis there is generally a marked distortion of the trigon owing to traction of a shortened tuberculous ureter, the ureteral orifice of the good side occupying a position near the midline,

16. Young, H. H.: Changes in the Trigone Due to Tuberculosis of Kidney, Ureter and Bladder. Bridge Formation and Floating Trigone, Surg., Gynec. & Obst. 26:608 (June) 1918.

while the opposite tuberculous ureteral ridge is drawn outward on the bladder wall (Case 8971).

The progressive steps of the invagination of the trigon into the ureteral orifice due to traction by a shortened ureter have been followed in our series. The first step is seen in Case 2438, in which the ureteral orifices lay equally distant from the midline on hypertrophied ridges, the right orifice appearing normal, but the left was a transverse slit lying across the ureteral ridge.

The next step is the invagination of the ureteral ridge into this transverse slit as is shown in Case 5541. Here the trigon is markedly distorted, the left ureteral orifice occupying a position almost in the midline while the right orifice is not visible, the corner of the trigon



Fig. 8.—A shortened tuberculous ureter causes the corner of the trigon to stand out as a wedge, which disappears under a crescent-like fold of mucosa. With each inspiration a stream of pus is seen to come from under this fold (Case 5541).

being drawn upward and outward with a pronounced thickening of the ureteral ridge which disappears under a crescent-shaped fold of mucosa with pouches on each side. With each inspiration a stream of pus is seen to come from under this fold of mucosa (Fig. 8).

In Case 3890, starting from the normal right ureteral orifice and passing toward the left, the ligamentum interuretericum becomes progressively more and more pronounced and is finally greatly elevated, the whole corner of the trigon standing out as a wedge-shaped ridge of considerable prominence running into the left ureteral orifice. As the patient expires, the corner of the trigon is drawn up into the ureter,

and as he inspires, it descends at least 1 cm., but even on deep inspiration the ureteral orifice is still invaginated. As the patient lies on his back the prominent trigonal ridge slides back and forth in the ureteral orifice synchronously with the respiration. On inspiration, the diaphragm descends, and along with it the kidney and shortened tuberculous ureter; and vice versa, on expiration the ureter draws the trigon up in this remarkable case, the first on record. The ureteral orifice is held up as a prominent concave fold upon this ridge, in front of and behind which is quite a deep pouch, probably 2 cm. deep. Following a left nephrectomy the cystoscopic picture was markedly changed. The left ureteral orifice lay on a hypertrophied ridge which was much less prominent than before, the orifice appeared a little more contracted than normal, and there was no urine coming from it. There was no movement of this corner of the trigon on respiration and no invagination.



Fig. 9.—The trigon is elevated above the surrounding bladder mucosa like a suspension bridge, supported only at the three corners. The cystoscope is in position, with fulgurating wire separating points of attachment of trigon (Case 3565).

A later stage is the ulceration of the depressed portions of the bladder leading to the complete undermining of the elevated trigon which thus forms a bridge of healthy tissue across the newly formed tuberculous cavity. In Case 5194, following a right nephrectomy, there was no relief from vesical symptoms, the bridge causing an obstruction to urination, vesical pain, frequency of urination (voiding every ten to fifteen minutes) with marked burning in the bladder. Eight months later, through a suprapubic incision the right half of the bridge was removed with an electric cauter, the left half not being disturbed. Though a marked vesical tuberculosis was present, there was a tempo-

rary improvement of symptoms. (Five years later the patient reported that he was still able to carry on his business, and had gained 40 pounds in weight, but had complete incontinence.)

In a similar case (Case 3565) the entire trigon was found by cystoscopy to be detached, except at its three corners, and floating (Fig. 9). It was removed, the attachments at the three corners being destroyed with a rongeur cystoscope and fulguration, and a week later the trigon, which was free in the bladder, was removed with forceps through a cysto-urethroscope. The patient's condition was distinctly improved as micturition was less difficult and frequent, but he had a small amount of residual urine and complained that he had to strain to pass the last urine. (He died of pulmonary tuberculosis two years later.)

No similar cases have been recorded in the literature since (or before) our publication, but it seems very evident that tuberculosis may produce not only marked thickening but also shortening of the ureter, and that this in turn may make traction upon the vesical end of the ureter and trigon, leading to invagination of the margin of the ureteral orifice and elevation of the trigon on that side; leaving the bladder depressed around it. Tubercle bacilli coming from the ureter naturally find easy lodgment in these vesical pouches, while the greatly elevated ureteral ridge and trigon remain uninvolved. Ulceration in the pouches may lead to undermining of the trigon and separation from the bladder.

It is interesting to note the changes in micturition which have occurred as a result of these transformations of the trigon. Urination is apparently normal as long as the trigon is not detached, but when the trigon becomes pathologically dissected free from the bladder muscle, micturition seems to become less free and residual urine is present. In one case this persisted after operative removal of the "floating trigon." Was this abnormality of micturition due to the absence of the trigon and consequent lack of muscle to open the vesical orifice and provide free urination? We think so.

TRIGONAL CHANGE FOLLOWING NEPHRECTOMY

The changes in the trigon following nephrectomy, when there is not a shortened tuberculous ureter, are shown in Case 3597. The trigon was normal preceding a right nephrectomy for tuberculosis, but two years later the right ureteral orifice was retracted, round and gaping, and was pulled over by the function of the other ureter, as the contraction of the trigon undoubtedly extended up to the orifice of the right side, and the swirl of urine from the left swept over it and appeared to come from it.

dice; mild dyspepsia was mentioned occasionally. They are living normal lives, and working; they do not require the services of a physician. Nine patients are in fair health only. This means that they have more attacks of abdominal pain with or without jaundice. Two patients have had occasional attacks of pain, chills, fever and jaundice, but little dyspepsia. They are, however, living fairly comfortably, with one exception, a man, aged 61. Two patients (4.8 per cent) have not been heard from.

INTRAHEPATIC JAUNDICE (SIXTH SERIES)

In the four cases of biliary cirrhosis in this series, cholecystogastrostomy had been performed. The average history was of ten months' duration. Jaundice was constant and the average duration was nine and seven-tenths months. In each instance, besides definite and marked cirrhosis, the regional lymph nodes were markedly enlarged. An operation had been performed previously on only one case. The gallbladder had been drained and stones removed fourteen years before, with complete relief until one month before the patient presented herself for treatment. The immediate results were good, and one and a half years after operation she was much improved, but occasionally experienced slight jaundice and mild dyspeptic attacks in which "gas" was a prominent symptom. The three remaining patients have not been heard from.

MISCELLANEOUS (SEVENTH SERIES)

There were three cases in this series: congenital absence of the common duct; obstruction of the common duct and duodenum due to perforated duodenal ulcer, and jaundice from undetermined cause.

The first case was that of a baby girl, aged 5 months, who had been jaundiced since birth. There was general adenopathy and the liver and spleen were much enlarged. At operation the gallbladder was found buried in the liver and the common duct extended only to the gallbladder. There was a moderate amount of free bile-stained fluid in the abdomen and the liver and spleen were large. The side of the gallbladder and the common duct were anastomosed to the duodenum. The child died three days after the operation. At necropsy no connection was found between the bile ducts and the duodenum. The duct ended as a blind pouch; it was this pouch which had been anastomosed to the duodenum. There was cirrhosis of the liver, graded 1, and hypertrophy of the spleen. The cause of death was peritonitis and pneumonia.

In the second case, that of a woman, aged 49, there had been typical recurring attacks of biliary colic with nausea and vomiting, but without jaundice for six years. Two years previously the gallbladder had been drained, with relief for six months. Then a biliary fistula developed,

with return of the former symptoms. At operation, a large perforating duodenal ulcer was found which had caused marked deformity with obstruction of the duodenum and the common duct. The gallbladder was small and showed evidence of chronic cholecystitis. The stomach was moderately dilated. The biliary fistula was excised, and cholecystoduodenostomy and posterior gastro-enterostomy were performed. The patient recovered uneventfully and six years after the operation considered herself completely cured.

In the third case, that of a man, aged 62, indefinite dyspepsia had existed for four years, and six weeks prior to examination painless jaundice with nausea and vomiting had developed. At the time of operation the dilatation of the common duct was graded 2; stones could not be found. Enlargement of the regional lymph nodes was graded 2. The pancreas and ampulla were normal and the liver was in good condition. No cause could be found for the jaundice and a diagnosis of "jaundice of undetermined origin" was made. Cholecystogastrostomy was performed. The patient recovered uneventfully and left the clinic with the jaundice practically cleared. He returned eight months later with a small ventral hernia, of no consequence, and reported marked improvement. He had not been jaundiced since the operation. Occasionally he had been troubled with slight dyspepsia.

SUMMARY OF POSTOPERATIVE RESULTS

In the 137 cases discussed, there were nine of contraction of the stoma. Partial or complete contraction of the stoma occurred in seven of the forty-seven cases in which hepaticoduodenostomy had been performed for stricture. Return of symptoms occurred from one to six months after operation, the average being four and two-tenths months. Reconstruction of the stoma over a rubber tube was carried out in each instance. One patient was apparently cured and died from acute gastric obstruction one and a half years after operation. Five patients are still living from two to four and a half years after operation, the average being two and nine-tenths years. Two of the five have been completely relieved of their former trouble for four and a half and three years, respectively. Three are much improved, but occasionally have slight attacks of pain, chills, fever and jaundice, although not severe enough to require the services of a physician. There were two other cases in which the stoma of the anastomosis contracted and produced obstruction to drainage of bile. In one, cholecystogastrostomy had been performed for obstructive jaundice due to carcinoma of the pancreas. After two months there was a return of symptoms, requiring reconstruction of the contracted stoma. In the other case cholecystoduodenostomy had been performed for obstructive jaundice caused by pancreatitis. Return of symptoms necessitated enlargement of the contracted stoma.

BLOOD IN THE CEREBROSPINAL FLUID

RESULTANT FUNCTIONAL AND ORGANIC ALTERATIONS IN THE CENTRAL NERVOUS SYSTEM *

A. EXPERIMENTAL DATA

CHARLES BAGLEY, JR., M.D.
BALTIMORE

This work has been done with the hope of experimentally producing lesions simulating those occurring in human beings when a small amount of blood escapes into the subarachnoid space.

METHODS AND MATERIAL

Eighteen adult dogs (exact age unknown) and twenty-six puppies (five litters), all less than 10 days old, were injected with whole blood. An average pup from each litter was used as a control.

The whole blood was obtained from the vein in the leg of the adult dogs and from the longitudinal sinus of the pups. Free mixture of the blood and cerebrospinal fluid was desired, and the blood was slowly injected into the cisterna magna, into the subarachnoid space over the cerebral hemisphere and in a few instances, into the cerebral ventricles.

The work was started on adult dogs with frequent injections of from 0.5 to 2.5 cc. of blood. Larger amounts could not be injected into the cisterna magna without causing serious respiratory symptoms, but in a few instances, as much as 5 cc. was tolerated over the cerebral cortex. In the beginning, when adult dogs were being used, it was thought that repeated injections at short intervals would be required to produce a disturbance comparable to that observed in human beings with bloody cerebral spinal fluid; for this reason, some of the earlier dogs received as many as six injections. In the later experiments with young pups, it was found that a single injection would sometimes produce symptoms; therefore, most of these pups received only one or two injections.

Ether anesthesia was used in the adult dogs. Morphine, $\frac{1}{8}$ grain (0.01 Gm.) was given hypodermically about a half an hour before the administration of ether. Chloroform without morphine was used in anesthetizing the pups.

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* From the Neurological Laboratory of the Henry Phipps Psychiatric Clinic, Johns Hopkins University, with the assistance of the Epilepsy Medical Research Fund.

When the animals died or were killed, autopsies were performed. To avoid possible injury of the meninges in the removal of the brain, the skull containing the brain was sectioned with a fine saw and then immersed in 10 per cent formaldehyde. By this method any portion desired for photography or microscopic study could be exposed in the fresh state and the entire brain easily brought into contact with the fixing fluid. The tissue was embedded in paraffin unless the dura was included in the blocks, in which case celloidin was used. Hematoxylin and eosin stain was used.

CLINICAL COURSE

Immediately after the injection, the adult animals were restless, spastic and recovered from the narcosis slowly. At times the spastic extremities were active; in some cases, the movements simulated running. At other times, there were atypical convulsive seizures with frothing at the mouth. The day following the injections the animals were usually dull, but walked about the cage and took food. After the injections, the dogs were kept under observation in the laboratory from one to three hours; then they were returned to the animal room. Daily visits were made to the animals, and every few days they were brought into the laboratory and allowed to play about under observation from one to three hours. In this way, it was possible to record symptoms which varied from difference in behavior to severe convulsive seizures.

The clinical course in most of the adult dogs was short because of the brief intervals between the injections. Many of them died within a few days after the last injection with gradually increasing debility marked chiefly by emaciation and irritability. They were hypersensitive and would cry out if handled. One of the adult dogs was given four injections into the cisterna magna over a period of one month, and was kept under observation thirty days after the last injection. During this period, there was gradually increasing weakness; because of the poor physical condition, the dog was killed with chloroform. A section from the base (fig. 3) shows chronic checking.

The most striking clinical course was seen in the younger dogs. This was first noticed in the behavior of the animals that had received injections as compared with the controls. After recovery from the immediate effects of the injection, the pups were less active, so that the puppies that had been treated could be picked out of the litter by the fact that they retired to a corner of the room and showed little of the characteristic tendencies of such animals to play. When stirred to activity, they would lose interest much more quickly than the controls.

In spite of the fact that the puppies ate well, they were generally smaller and markedly thinner. The difference in size between the control animals and animals that had received injections was seen in a

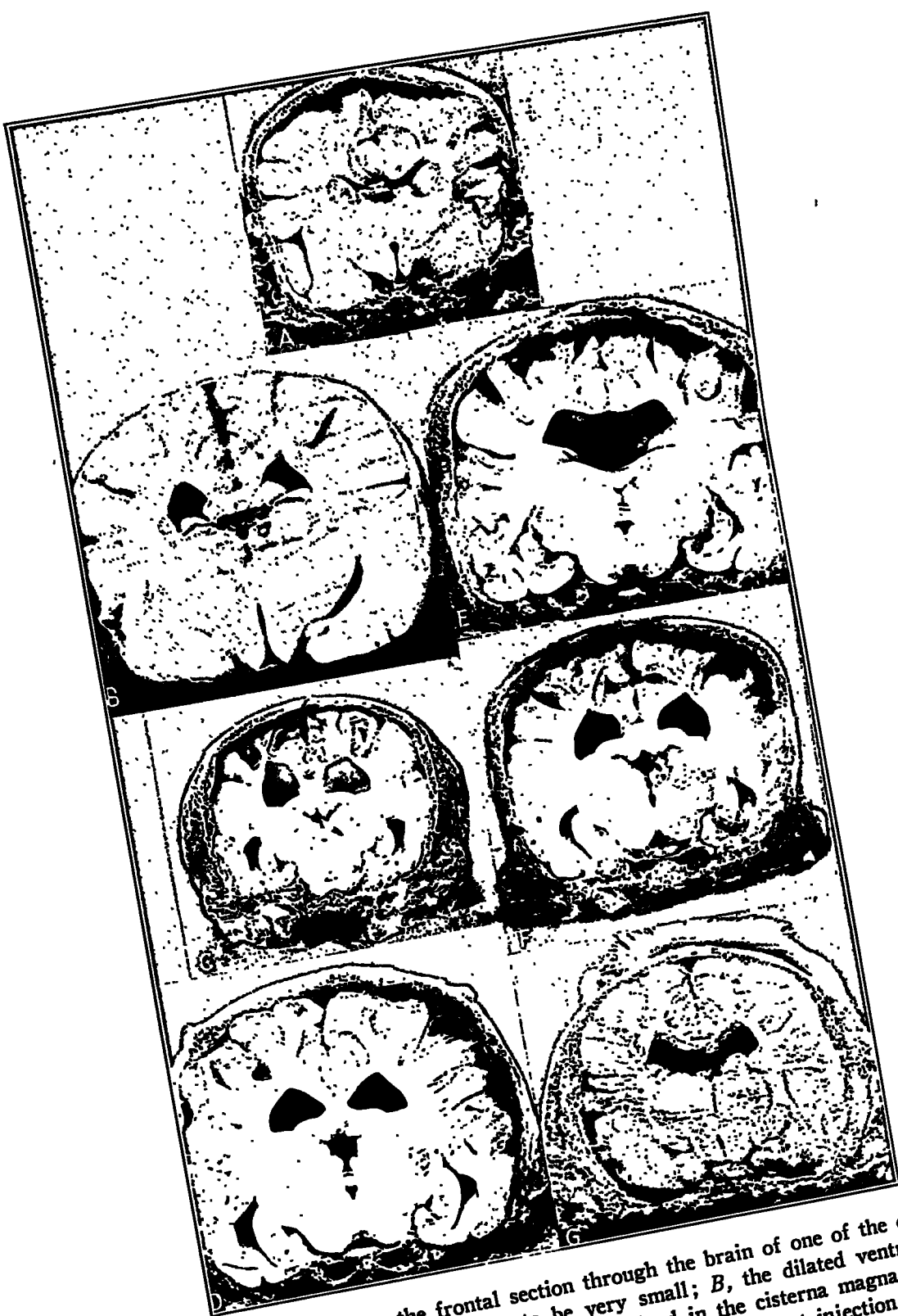


Fig. 1.—*A* indicates the frontal section through the brain of one of the control pups showing the normal ventricle to be very small; *B*, the dilated ventricle of adult dog 10 which received six injections of blood in the cisterna magna over a period of thirty-nine days and was killed two days after the last injection; *C*, the brain of pup 35 which received three injections of blood over the right cortex and two in the cisterna magna over a period of forty-two days and was killed twenty-one days after the last injection; *D*, the brain of pup 37 which received two injections of blood over the right cortex and two in the cisterna magna over a period of forty-two days and was killed seven days after the last injection; *E*, the brain of pup 45 which received one injection of blood in the cisterna magna and was killed twenty-one days later; *F*, the brain of pup 47 which received two injections in the cisterna magna over a period of seven days and was killed ten days after the last injection; *G*, the brain of pup 70 which received 1.25 cc. of blood in the cisterna magna and died sixty-two days later.



Fig. 2.—A section taken from the base of an adult dog which received four injections of blood from 1 to 1.5 cc. in amount into the cisterna magna over a period of seventeen days. The animal was killed two days after the last injection. The meninges were thickened and the seat of active cell proliferation.

pup (35, table 4) that had had five injections, three over the cerebral cortex and two at the base over a period of forty-two days. The first injection was given when the dog was 10 days old. When killed sixty-three days after the first and twenty-one days after the last injection, the general condition was fair. All the organs were normal except the brain. The dilatation of the ventricles was definite when compared with that of the control pup. Examination of the meninges showed chronic thickening over the base and cortex similar to that shown in figure 11. Another striking example was seen in a pup (54, table 1) which when 3 months old weighed scarcely half as much as the control. This pup had general convulsive seizures almost two months after the

TABLE 1.—*Protocols of Pups in Which Convulsions Occurred*

| Date | Amount Injected | Remarks | Lesions |
|----------------|---------------------------|--|--|
| Pup 46 | | | |
| April 23, 1926 | 1 cc. in cisterna magna | Satisfactory recovery | Meningeal thickening more marked over cerebral cortex where there is some scarring |
| June 7 | | Severe general convulsions | |
| June 9 | | Died | |
| Pup 50 | | | |
| April 26, 1926 | 1 cc. in ventricle | Recovery | Meningeal thickening over cortex, chiefly at sulci; none over base |
| May 14 | 3.5 cc. over left cortex | Recovery | |
| May 17 | 2.5 cc. over right cortex | Recovery | |
| June 9 | | Severe convulsive seizures; died | |
| Pup 54 | | | |
| Jan. 21, 1927 | 0.5 cc. in cisterna magna | Respiratory embarrassment | Meningeal thickening at base and some areas of the cortex with cortical scarring |
| Feb. 11 | 0.8 cc. in cisterna magna | Very limp for some minutes following injection | |
| May 2 | | Severe general convulsive seizures | |
| July 13 | | Series of general convulsive seizures; died | |
| Pup 56 | | | |
| Feb. 2, 1927 | 0.5 cc. in cisterna magna | Rapid recovery | Brain not sectioned; in poor condition when received in the laboratory |
| Feb. 4 | 1 cc. in cisterna magna | Rapid recovery | |
| May 18 | | General convulsive seizure | |
| May 19 | | General convulsive seizure | |
| Aug. 15 | | Died | |

last injection. Scattered areas of meningeal thickening were found during the examination of the brain, and there were areas of cortical scarring associated with the thickening (fig. 13).

Convulsive seizures immediately followed the injection in five of the ten adult dogs in which the blood was injected over the cerebral cortex, and in one of the four dogs in which blood was injected into the lateral ventricles. Convulsions did not occur immediately following the injections when young pups were used.

Four of the twenty-six puppies that received injections had convulsions after complete recovery from the immediate effects of the injection without indication of the seizure until a few minutes before the attack. The first pup (46, table 1) had a convulsion twenty-three days after the last injection; he survived for thirty-six hours, during which time there were a great many seizures. The second pup (50,

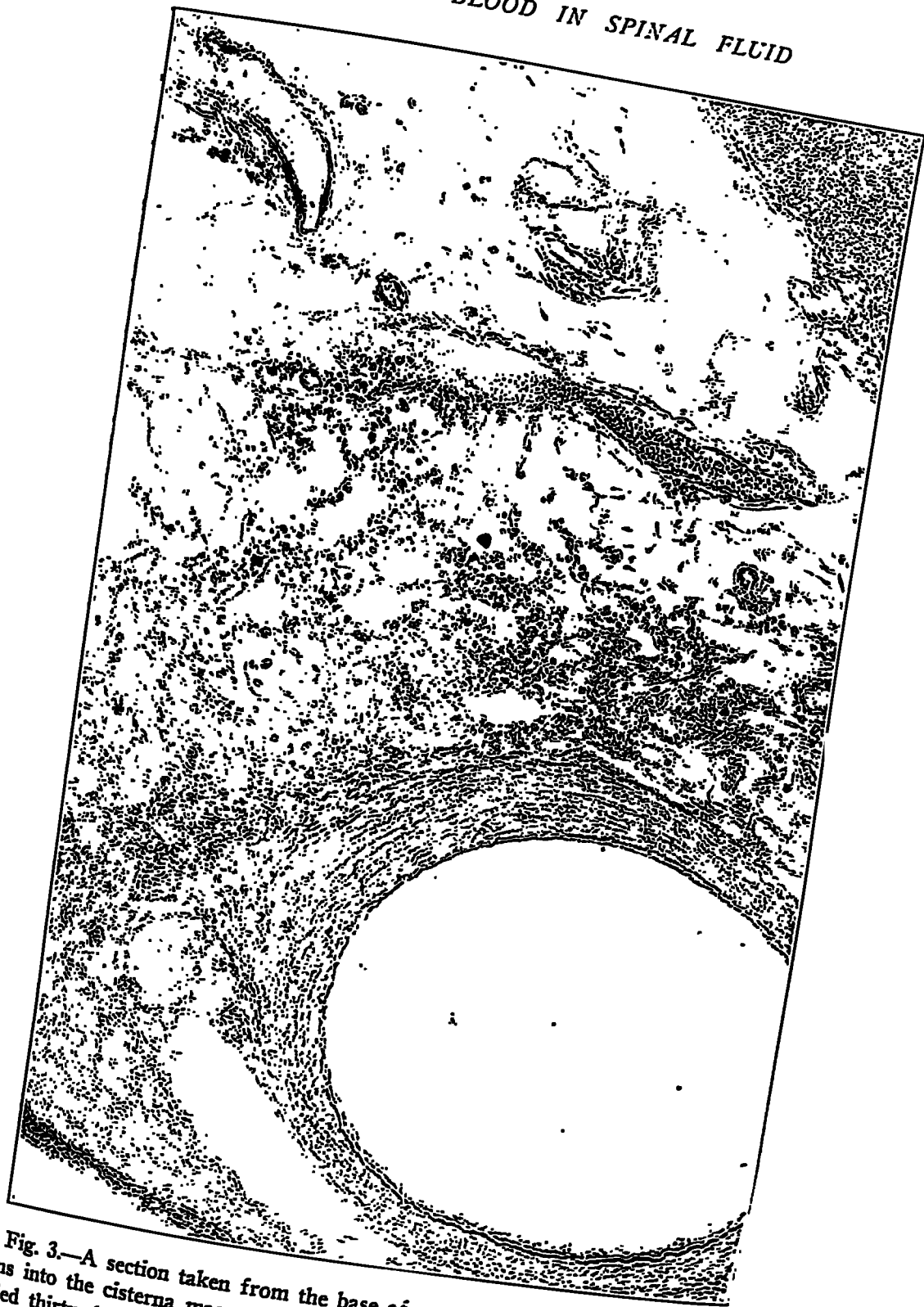


Fig. 3.—A section taken from the base of an adult dog which had four injections into the cisterna magna over a period of thirty-one days; the animal was killed thirty days after the last injection. In comparison with figure 2 there is a diminution of cells, but an increase of fibrous tissue. The fibrous tissue contains a number of pigment-loaded phagocytes.

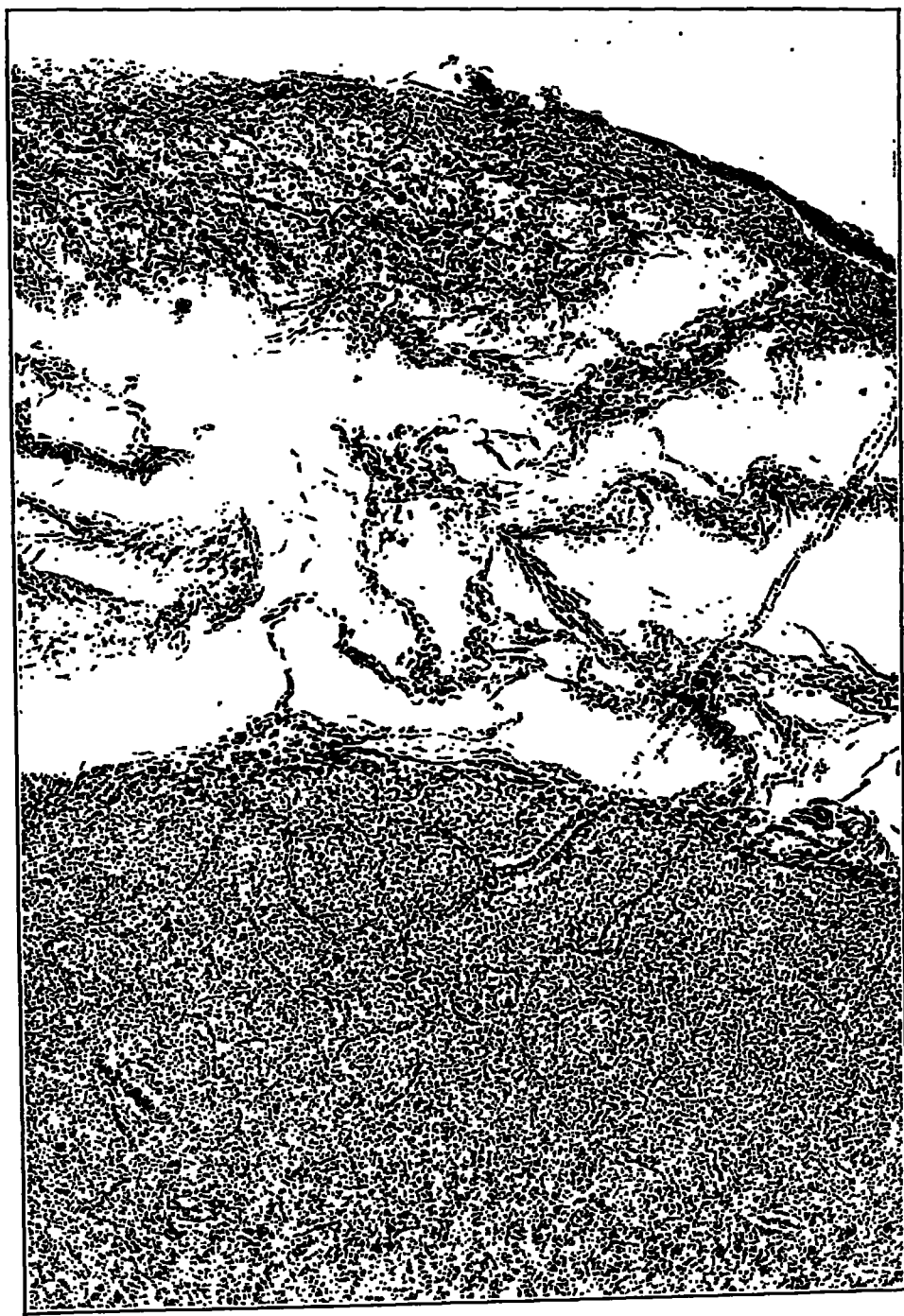


Fig. 4.—A section taken from the crest of a gyrus adjacent to the longitudinal sinus of the same dog as figure 3 showing an increase of fibrous tissue elements.

table 1) had its first convulsion forty-five days after the last injection; this seizure was followed by many others and he died during the same day. In the third pup (54, table 1), the first seizure occurred eighty days after the last injection; from this it recovered promptly and remained fairly well for seventy-two days when, without warning, there was a second series of convulsions in which the animal died. The fourth pup (56, table 1) had single convulsions ninety-three and ninety-four days after the last injection; it recovered from these. It was kept under observation eighty-seven days, during which time it did not have convulsions; but it was aggressive and ill-tempered, and was killed in a fight with another dog.

The seizures were all similar, starting with fine twitchings of a muscle group, usually the face and then spreading over the entire body.

TABLE 2.—*Protocols of the Pups with General Muscle Twitching*

| Date | Amount Injected | Remarks | Lesions |
|---------------|---------------------------|---|--|
| Pup 59 | | | |
| Feb. 28, 1927 | 0.8 cc. in cisterna magna | Satisfactory recovery | Moderate meningeal thickening at base |
| March 9 | 0.5 cc. in cisterna magna | Recovery | |
| March 28 | 1 cc. in cisterna magna | Recovery | |
| May 6 | | Weak and sick in appearance; twitching | |
| May 8 | | Weak with irregular twitching of all muscles, rhythmical twitching of the right hind leg; head drawn to right | |
| May 9 | | Irregular twitching of all muscles, rhythmical twitching of right fore-leg; died | |
| Pup 61 | | | |
| Feb. 28, 1927 | 1.5 cc. in cisterna magna | | Very slight meningeal thickening at base |
| March 28 | | Very poor condition; twitching, unsteady, restless and listless | |
| March 29 | | Died | |

The animal would soon lose consciousness and fall. The facial expression before loss of consciousness showed marked anxiety. Following the attack, the animal was dull and stupid and remained so between the seizures when they occurred in series.

In addition to the four pups which developed convulsions, two were observed forty-three and twenty-nine days, respectively, after the last injection, with severe twitchings involving all the muscles of the body without loss of consciousness. In one of these, pup 61 (table 2), the twitchings continued throughout the day; the dog was greatly weakened and died during the night. Another, pup 59 (table 2), previously well, had twitchings for three days, and on the morning of the third day was weak and twitched constantly; he died before noon. On the lateral surface of the tongue, there was a laceration which was perhaps due to biting during a general convulsive seizure in the night.



Fig. 5.—A section from the mesial wall of the hemisphere adjacent to the falx showing meningeal thickening at the top of a sulcus. The dark cells are phagocytes filled with blood pigment. At *A* two pigment filled phagocytes are seen in the perivascular space.



Fig. 6.—A section taken from dog 10 showing the matting together of the meninges, which is the forerunner of cortical alterations.

Convulsions or muscle twitchings were not observed in six other pups (table 3) which died from nine to sixty-three days after the injections.

In addition to the foregoing twelve puppies that died as the result of the injection, eight pups that had received injections and two controls were killed for histologic study when about half grown. Six of the pups that received injections are living and apparently well. More than one year had elapsed since the last injection was made into the six living puppies. At this time these animals do not show any ill effects resulting from the injection. They will be killed for histologic

TABLE 3.—*Protocols of the Pups Which Died Without Having Had Convulsions or Muscle Twitchings*

| Date | Amount Injected | Remarks | Lesions |
|----------------|----------------------------|-----------------------|--------------------------------|
| Pup 32 | | | |
| March 26, 1926 | 8 cc. over right cortex | Satisfactory recovery | Meningeal thickening |
| April 4 | | Died | over cortex |
| Pup 33 | | | |
| March 12, 1926 | 1 cc. over right cortex | Satisfactory recovery | Moderate degree of |
| March 26 | 2.5 cc. over right cortex | Satisfactory recovery | meningeal thickening |
| April 4 | | Died | over the right and left cortex |
| Pup 34 | | | |
| March 12, 1926 | 1 cc. over right cortex | Satisfactory recovery | |
| March 23 | 3 cc. over right cortex | Satisfactory recovery | Meningeal thickening |
| April 16 | 4 cc. over right cortex | Satisfactory recovery | over cortex with some |
| April 20 | 3 cc. over right cortex | Satisfactory recovery | scarring |
| April 28 | 2 cc. over right cortex | Satisfactory recovery | |
| May 13 | | Died | |
| Pup 36 | | | |
| March 19, 1923 | 3 cc. over right cortex | Satisfactory recovery | No section; brain in |
| March 29 | 3 cc. over right cortex | Satisfactory recovery | poor condition when |
| April 16 | 4 cc. over right cortex | Satisfactory recovery | received in the lab- |
| April 20 | 3 cc. over right cortex | Satisfactory recovery | oratory |
| April 28 | 2.5 cc. over right cortex | Slow recovery | |
| May 17 | | Died | |
| Pup 44 | | | |
| April 23, 1926 | 1 cc. in cisterna magna | Satisfactory recovery | No section; brain in |
| June 9 | | Died | poor condition when |
| | | | received in the lab- |
| | | | oratory |
| Pup 70 | | | |
| March 28, 1927 | 1.25 cc. in cisterna magna | Satisfactory recovery | Moderate degree of |
| May 30 | | Died | meningeal thickening at base |

purposes when full grown. Of the five controls, two that were killed for histologic study seemed entirely normal at the time they were killed, and the three remaining control dogs are living and well.

LESIONS

The study of the brains of the animals that died a short time after the last injection showed grossly blood staining of the portion of the meninges with which blood had come in contact and thickening of the stained membrane. In the brains removed long after the last injection, the gross appearance varied from slight thickening of the meninges to normal. Frontal sections through the ventricles of the forebrain showed a degree of dilatation of the ventricles varying from slight to well



Fig. 7.—A section of cortex adjacent to a sulcus in which there is matting of the meninges. Active cell proliferation within the cortex is shown.



Fig. 8.—A further stage of cortical scarring following the cell proliferation as shown in figure 7.

marked. In the adult dogs, ventricular dilatation was less frequent than in the case of the pups. Of the seven adult dogs given one or more injections over the cortex and of the seven adult dogs given one or more injections into the cisterna magna, only one dog (10, table 4) showed a well marked dilatation of the ventricles (figs. 1-3). This animal was given six injections of blood into the cisterna magna over a period of thirty-nine days and was killed two days after the last injection.

TABLE 4.—*Protocols of Animals with Dilatation of the Ventricles*

| Date | Amount Injected | Remarks | Lesions |
|----------------|----------------------------|-----------------------|---|
| Dog 10 | | | |
| Jan. 23, 1925 | 1 cc. in cisterna magna | Satisfactory recovery | Marked meningeal thickening of meninges, at base and in some areas of cortex |
| Feb. 4 | 1.5 cc. in cisterna magna | General convulsion | |
| Feb. 9 | 1.5 cc. in cisterna magna | Slow recovery | |
| Feb. 18 | 1.5 cc. in cisterna magna | Satisfactory recovery | |
| March 1 | 2 cc. in cisterna magna | Slow recovery | |
| March 8 | 1 cc. in cisterna magna | Slow recovery | |
| March 5 | | Killed | |
| Pup 31 | | | |
| March 12, 1926 | 1.5 cc. over right cortex | Satisfactory recovery | Marked meningeal thickening over base and cortex |
| March 29 | 2.5 cc. over right cortex | Satisfactory recovery | |
| April 12 | 2 cc. in cisterna magna | Satisfactory recovery | |
| April 20 | | Killed | |
| Pup 35 | | | |
| March 17, 1926 | 3 cc. over right cortex | Satisfactory recovery | Moderate meningeal thickening at base, not much over cortex |
| March 24 | 0.5 cc. over right cortex | Slow recovery | |
| March 29 | 2.5 cc. over right cortex | Satisfactory recovery | |
| April 16 | 1 cc. in cisterna magna | Satisfactory recovery | |
| April 28 | 2.5 cc. in cisterna magna | Satisfactory recovery | |
| May 10 | | Killed | |
| Pup 37 | | | |
| March 17, 1926 | 3 cc. over right cortex | Satisfactory recovery | Marked meningeal thickening at base and moderate over cortex, especially at sulci |
| March 26 | 3 cc. over right cortex | Satisfactory recovery | |
| April 12 | 1 cc. in cisterna magna | Satisfactory recovery | |
| April 28 | 1.5 cc. in cisterna magna | Satisfactory recovery | |
| May 5 | | Killed | |
| Pup 45 | | | |
| April 23, 1926 | 2 cc. in cisterna magna | Satisfactory recovery | Very slight meningeal reaction over base |
| May 14 | | Killed | |
| Pup 47 | | | |
| April 23, 1926 | 1 cc. in cisterna magna | Satisfactory recovery | Moderate degree of meningeal thickening at base |
| April 30 | 2 cc. in cisterna magna | Satisfactory recovery | |
| May 10 | | Killed | |
| Pup 70 | | | |
| March 23, 1927 | 1.25 cc. in cisterna magna | Satisfactory recovery | Moderate degree of meningeal thickening at base |
| March 29 | | Died | |

Six of the nineteen puppies which had received injections and on which autopsies have been performed had definite dilatation of the ventricles (fig. 1). As shown by the protocols, all of the puppies with dilated ventricles had been given one or more injections into the cisterna magna; in addition, in some injections were given over the cortex. Two of the pups (45 and 70, table 4) received only one injection, one 2 cc. and the other 1.25 cc. of blood into the cisterna magna. One of the pups was killed twenty-one days after the last injection. The dilatation of the ventricles was always associated with meningeal thickening. Clinically, the animals did not show any evidence of the dilatation.



Fig. 9.—Active cell proliferation in the meninges covering the optic nerve. The section was taken from dog 10.

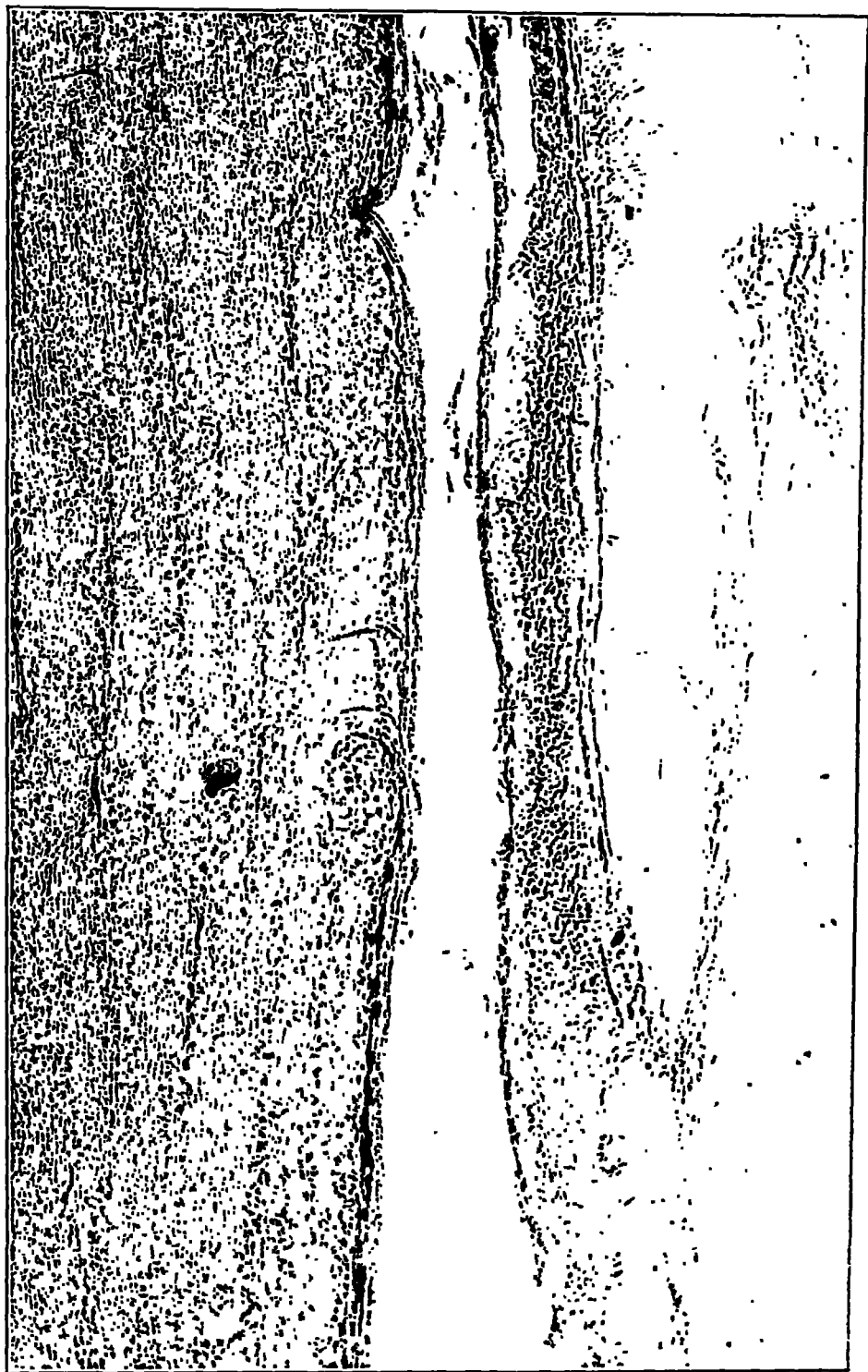


Fig. 10.—A section taken from the optic nerve of one of the control mice showing the normal meningeal coverings of the nerve.



Fig. 11.—A section from the base of the brain of pup 46 which died following convulsive seizures forty-seven days after an injection of 1 cc. of blood in the cisterna magna. There is marked meningeal thickening with cell infiltration.

The microscopic study of the brains showed meningeal thickening where blood came in contact with the membranes. In the acute stage, that is in the dogs killed soon after the last injection, the meninges showed marked cell proliferation. In figure 2, the thickened membrane is shown at the base of the brain of a dog that had been given four injections into the cisterna magna over a period of seventeen days and was killed two days after the last injection. The chronic stage of this condition is shown in figure 3, a photomicrograph from the base of the brain of an animal killed thirty-three days after the last injection. During the thirty-three days, the clinical condition was not satisfactory in that the animal ate poorly and was very weak.

This condition is not limited to the base of the brain as shown in figure 4, which is an illustration of a section taken from the same dog over the crest of the gyrus adjacent to the longitudinal sinus. The meningeal thickening is often marked at the site of sulci diminishing as the crest of the sulcus is reached. In figure 5, taken from dog 10 (table 4), the meningeal thickening at a sulcus is seen. The heavily stained cells are phagocytes filled with blood pigment. The pigment-laden cells are found even in the chronic state of the meningeal thickening secondary to the injection of blood and are useful in the microscopic examination of the specimens, as is blood-staining in the gross appearance in determining the areas of the meninges with which the blood had come in contact.

In figure 5, at *A* two pigment filled phagocytes are seen in a perivascular space well below the surface of the cortex, indicating an early stage of cortical alteration. This cortical alteration is frequently secondary to a condition seen in figure 6, where it is shown that the meningeal reaction has progressed to a point of matting together of the membranes in a sulcus, entirely obliterating the normal meningeal spaces. With a beginning cortical alteration, as seen in figure 5, active cell proliferation (fig. 7) ensues, which progresses for a time and results in fibrous tissue deposit constituting a scar, as shown in figure 8.

The meningeal reaction extends to the membranes covering the optic nerve, as shown in figure 9, a photograph of a section of the optic nerve and its coverings taken from dog 10 as compared with the same structures in figure 10, taken from one of the control puppies.

In the pups that presented symptoms and in those that died, meningeal thickening as shown in the previous sections was observed. For example, in figure 11, taken from the base of the brain of pup 46 (table 1), the meninges are thickened and contain a large amount of fibrous tissue. A photograph (fig. 13) taken from the occipital pole of the brain of pup 54 shows the meninges of a sulcus in active cell proliferation extending into the cortex at the site of a blood vessel.



Fig. 12.—A section of the meninges from the base of pup 59 which died during convulsions forty-two days after receiving three injections of blood into the cisterna magna showing an increase of fibrous tissue elements.



Fig. 13.—A section taken from the occipital pole of pup 54 d. with moderate thickening in a sulcus with beginning cortical alteration.

CONCLUSIONS

Blood mixed with the cerebrospinal fluid of young and adult dogs produces neurologic disturbance varying from slight difference in behavior to severe convulsive seizures. Though some of the animals were severely affected by small quantities of blood mixed with the cerebrospinal fluid, others have survived more than a year, and are apparently normal.

Following the introduction of blood into the cerebrospinal fluid, there begins a reaction of the parts of the meninges which have come in contact with the blood. The meningeal reaction tends to subside and may disappear as the blood disappears from the fluid. After several weeks, the cell elements are less numerous in the meninges, but a large amount of fibrous tissue is present.

Late in the course of the meningeal reaction, changes in the structure of the cortex are observed.

Moderate dilatation of the ventricle not infrequently occurs following the introduction of blood into the cerebrospinal fluid of young pups. The condition may occur in adult dogs, but with less frequency.

These facts as applied to patients with bloody cerebrospinal fluid are discussed in part B of this paper.

This work has been carried on under the direction of Dr. Adolf Meyer. Dr. Frank Ford assisted in some of the experiments and Miss Cecelia Bisson in the making of the motion picture films, for the study of the behavior of the animals, and in making the illustrations for this paper.

BLOOD IN THE CEREBROSPINAL FLUID

RESULTANT FUNCTIONAL AND ORGANIC ALTERATIONS IN THE CENTRAL NERVOUS SYSTEM *

B. CLINICAL DATA

CHARLES BAGLEY, JR., M.D.

BALTIMORE

In a report concerning some experiments made to determine the effect of a relatively small amount of blood in the cerebrospinal fluid,¹ attention was directed to the acute and chronic symptoms resulting from the meningeal irritation caused by the blood. The present report concerns some experiences with bloody cerebrospinal fluid in patients ranging in age from a few days to 56 years who presented meningeal lesions similar to those produced in the experiments.

The sudden appearance of blood in the cerebrospinal fluid of the very young or of middle-aged persons is rare enough to excite one's curiosity as to the cause of the bleeding. The first part of this paper deals with the examination of the brains in some of the fatal cases and the lesions responsible for the blood.

REPORT OF CASES

CASE 1.—Venous plexus of cerebellar pia; drainage of cerebrospinal fluid without benefit.

Baby G. was admitted to the hospital when 16 days old. Labor was uncomplicated, and the child seemed normal in every way until 15 days old, when the mother noticed twitchings of the muscles of the body, drawing back of the head and rolling of the eyes. The following day there were several severe convulsions. Lumbar puncture, performed when the patient was admitted to the hospital, showed bloody cerebrospinal fluid. The drainage of this fluid did not improve the condition, and on the following day an opening was made in the right temporal region. When the dura was incised, there was little cerebrospinal fluid in the subarachnoid space, the cortical veins were dilated, and old blood was seen. The absence of cerebrospinal fluid was in striking contrast to the condition usually found in simple hemorrhages at birth. Drains were inserted beneath the dura. Following the operation there was not the usual free drainage of cerebrospinal fluid, and several lumbar punctures were made. In all of these punctures the fluid was bloody, and eighteen days after the operation it was concluded that a large blood clot was present. As there was no indication of the location of the supposed clot, further exploration was not attempted. treatment was

abandoned, and the child died fifty-one days after birth. Autopsy revealed a venous plexus covering the greater portion of the cerebellar cortex (fig. 1) and marked dilatation of the ventricle as shown in figure 2.

On section, the pia was seen to be much thickened and contained a great many dilated, thin-walled veins, as shown in figure 3. The sudden appearance of symptoms was due to rupture of a vein. Repeated punctures failed to clear the fluid because of recurrent bleeding from this source. The dilatation of the ventricles was due to the adhesions at the foramina of Magendie and Luschka. Hydrocephalus secondary to hemorrhage in the posterior fossa has been described by Arthur G. Jacobs² in the case of a new-born child with early evidence of hemorrhage. Seventy-five days after birth, suboccipital exploration by Dr. R. E. Semmes revealed extensive adhesions and arrested the condition.



Fig. 1 (case 1).—Greater part of the cerebellum is covered by a network of veins. Rupture of one of these veins was the cause of the hemorrhage fifteen days after birth.

CASE 2.—Venous plexus involving chiefly the occipital and cerebellar veins; extravasation of a small amount of blood from a cerebellar vein with signs of increased intracranial tension.

M. H., a girl, aged 20, had a history of normal development until the age of 6 years, when she had had a severe attack of measles, since which time she had not been strong. At the age of 12, she was extremely ill with influenza, and at that time a heart murmur with cardiac enlargement was found. At the age of 16, a murmur was first heard in the head. During the four years preceding the examination, headache was troublesome; it became severe after an attack

2. Jacobs, A. G.: Hydrocephalus Following Intracranial Hemorrhage, South. M. J. 19:669 (Sept.) 1926.

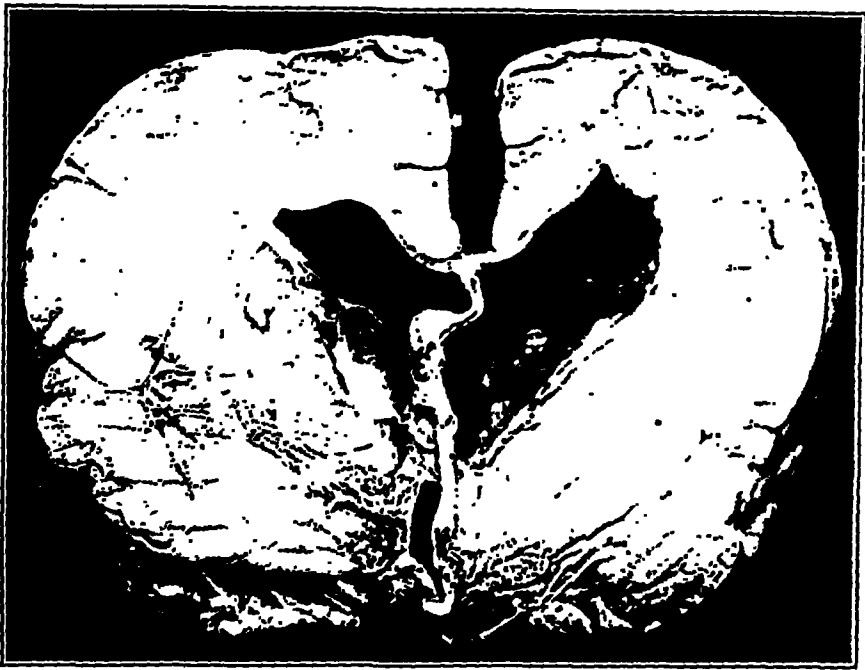


Fig. 2 (case 1).—The frontal section of the brain showing marked dilatation of the ventricles secondary to hemorrhage in the posterior fossa.

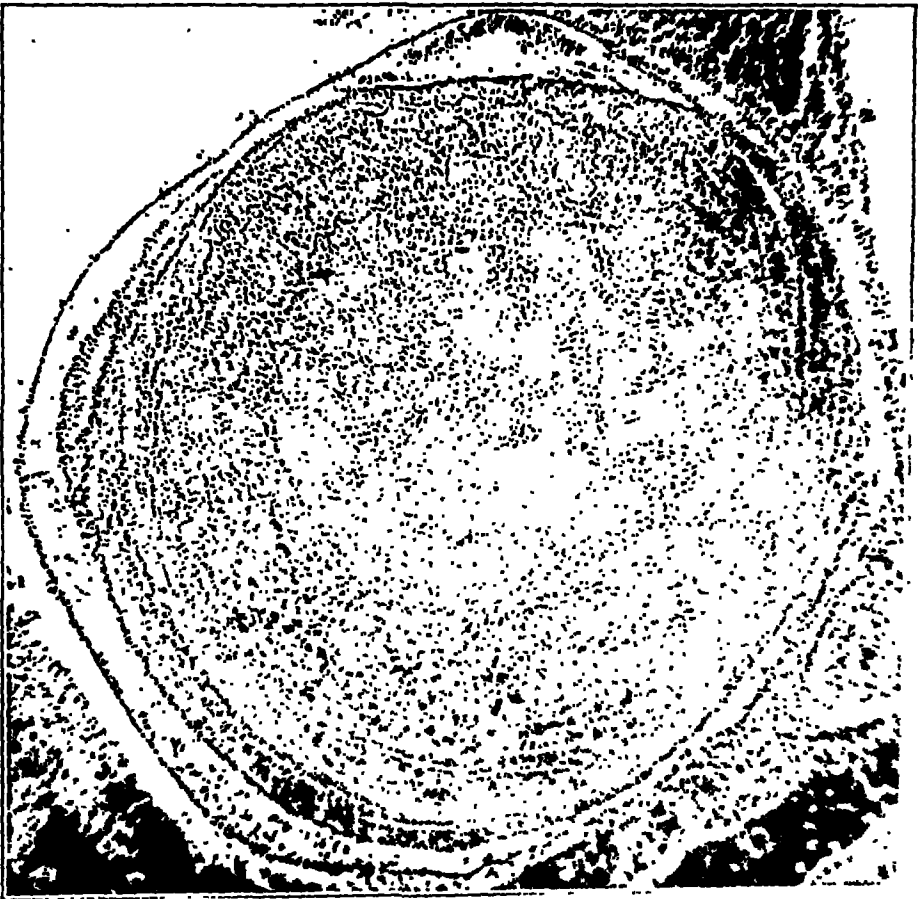


Fig. 3 (case 1).—Showing one of the many dilated follicles within the cerebellar cortex.

of otitis media twelve weeks before the examination, at which time a mild degree of choked disk was noted. These facts suggested the possibility of an abscess of the brain. Two weeks before the examination, while stooping to fasten her galoshes, she was suddenly aware of a brushing sound, which she thought was caused by some one passing her in the room. This was immediately followed by a severe headache, vomiting and dizziness. Lumbar puncture ten days later showed marked increase in pressure and evidence of a small amount of old blood in the cerebrospinal fluid. When examined four days after this puncture, the patient was stuporous but could be aroused. The examination revealed a loud systolic murmur over the precordium extending into the neck and a loud bruit over the entire head synchronous with the heart beat. There

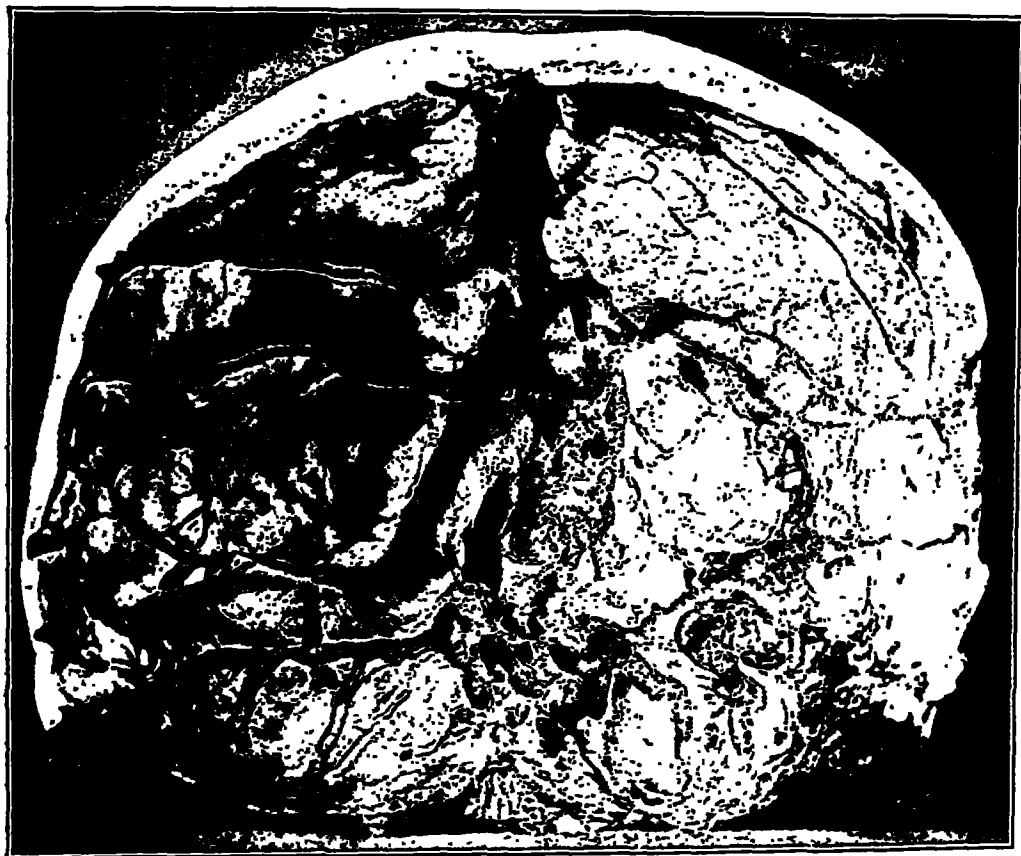


Fig. 4 (case 2).—The posterior part of the skull including the occipital and part of the parietal bones, showing the deep depressions corresponding to the greatly dilated venous sinuses and tributaries.

was marked spontaneous nystagmus and a high degree of choked disk. The diagnosis of a cerebral vascular lesion, exact type unknown, with leakage of blood into the cerebrospinal fluid was made. Because of the likelihood of exciting further bleeding, a lumbar puncture or a more radical operative procedure was not undertaken. Two weeks later, the patient was in a serious condition because of increased intracranial pressure, and she died twenty-four hours after an attempt at relief through a right subtemporal decompression.

Postmortem examination showed that the lesion involved chiefly the venous structure of the dura, resulting in deep channeling of the skull as shown in figure 4. In the left cerebellar pontile angle, several dilated and recently

thrombosed veins were seen (fig. 5). Sections of the area of extravasation showed several thin-walled veins (fig. 6). A large clot was not found; the marked increase in intracranial pressure was evidently due to the irritation of the bloody cerebrospinal fluid. Leakage had, no doubt, been occurring over a period of fifteen weeks, corresponding to the course of the final illness.

CASE 3.—Recurrent hemorrhage following rupture of an aneurysm of the anterior cerebral artery, with signs of increased intracranial tension.

E. S., a girl, aged 12, entered the hospital with a history of a sudden severe headache thirty-five days before admission. The headache was associated with vomiting. A week later, because of continuance of symptoms, she was admitted to the Western Maryland Hospital in Cumberland, and lumbar puncture at that time revealed bloody cerebrospinal fluid. Twelve days later, she was discharged from the hospital with marked improvement in symptoms, though she was rather dull and vision was blurred. Thirty-one days after the first attack of headache, she had a second severe attack with two general convulsive seizures, diplopia and



Fig. 5 (case 2).—Marked venous dilatation with recent thrombus in the cerebellar pontile angle.

badly blurred vision. Five days later, she was admitted to the Church Home and Infirmary, Baltimore, where I first saw her. At the time of admission, there was severe headache, vomiting and stupor (though she could be aroused) and a very high grade choked disk, with hemorrhages; the right pupil was larger than the left, and a loud cerebral bruit was heard over the entire head, but more distinctly in the temporal regions. When questioned, the child said that she had heard the murmur for a long time. Bloody cerebrospinal fluid was obtained on lumbar puncture. A right subtemporal decompression for relief of pressure was made, and the child died four days after operation. Figure 7 shows a large hemorrhage between the hemisphere extending into the left lateral ventricle. Microscopic study of this area showed an organized blood clot, the result, no doubt, of the bleeding which caused the original attack thirty-five days before admission to the hospital, a large amount of recent hemorrhage and an accompanying dilatation of the right anterior cerebral artery (fig. 8). Rupture of the aneurysm was the cause of the bleeding.



Fig. 6 (case 2).—A higher magnification of the vein in figure 5, showing the breaking down of the thin wall of the vein and recent thrombus.

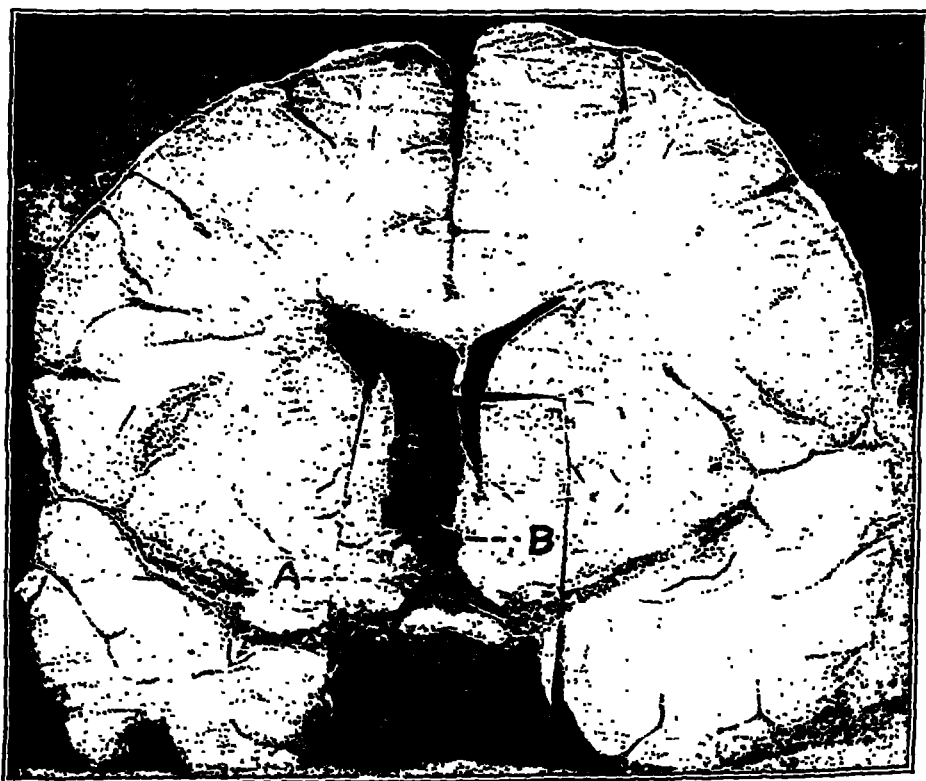


Fig. 7 (case 3).—Between the hemispheres there is a blood clot extending from the base into the left ventricle. At *A*, the cut end of the left anterior cerebral artery is seen; at *B*, an aneurysm of the right anterior cerebral artery.

CASE 4.—*Hemorrhage due to rupture of an aneurysm of the anterior cerebral artery. Death followed the initial rupture.*

C. B., a man, aged 37, previously in good health, was suddenly seized with severe headache and vomiting, followed almost immediately by coma. He died



section of the brain, as seen in figure 9, showed a bulbous enlargement of the anterior cerebral artery. Sections of this unruptured aneurysm are shown in figures 10 and 11. This lesion was not the source of the hemorrhage; a second small aneurysm of the artery ruptured subcortically. Small aneurysms of this type are frequently multiple.

CASE 5.—*Recurrent hemorrhage following rupture of an aneurysm of the anterior cerebral artery.*

M. H., a man, aged 41, was admitted to the hospital complaining of headache and weakness of the left side of the body. The illness began three months before admission with sudden loss of consciousness. Five weeks after the onset the patient again lost consciousness, and there was paralysis of the left side of the body; this gradually improved until the time of admission to the hospital. The

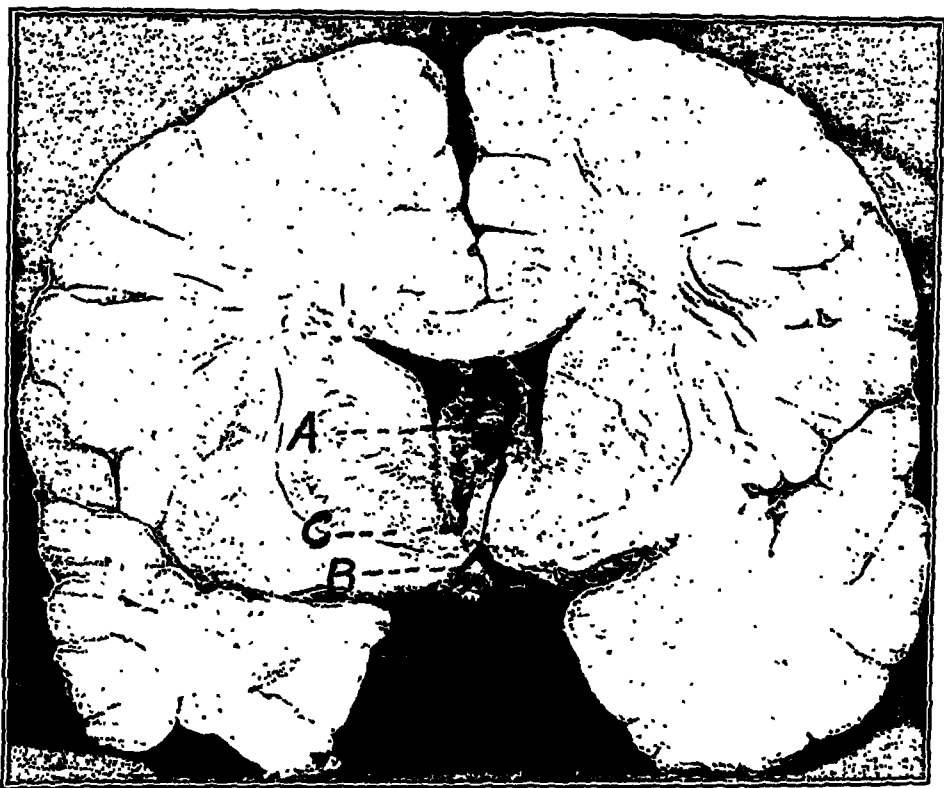


Fig. 9 (case 4).—*A* shows blood clot resulting from the rupture of a branch of the left anterior cerebral artery at *C*. *B* indicates aneurysm of the anterior cerebral artery unruptured, shown in figure 10.

examination showed partial hemiplegia of the left side and arteriosclerosis. The Wassermann test of the blood and spinal fluid was negative, and the spinal fluid contained 13 cells. Four days after admission to the hospital, the patient suddenly lost consciousness, but he improved during the following hour, at which time there was complete loss of power of all muscles of the left side of the body. He again lost consciousness and died two hours after the onset of the attack. The history did not mention a cerebral bruit, so that it is not possible to say whether or not one was present. Autopsy showed general arteriosclerosis, free blood over the right cerebral cortex and a partially organized blood clot at the base between the hemispheres of the brain anterior to the chiasm, as shown in figure 12.

Section of the blood clot showed an aneurysm of the right cerebral artery as shown in figure 13.

CASE 6.—*Recurrent hemorrhage in a patient at the age of 22, 42 and 44 years; large calcified mass at the site of the first hemorrhage and beginning calcification in the second with an aneurysm of the anterior cerebral artery; death two hours after the third hemorrhage.*





Fig 11 (case 4).—Higher magnification ($\times 125$) of *A* in figure 10, showing the abrupt termination of the elastic tissue.

was a mild degree of choking of both optic nerves. The roentgenogram showed a smooth, calcified mass 1 cm. above and not connected with the sella turcica (fig. 14). In the anteroposterior view, this mass was seen exactly in the midline (fig. 15). The patient said that at the age of 22 he had had a similar illness which had necessitated his remaining in bed for six weeks, but he had entirely recovered. This fact led to the opinion that the calcified mass shown in the roentgenogram had to do with the previous illness. The smooth external surface of the mass suggested calcification in a cyst, and tumor calcification was ruled out. Soon after the patient's admission, the symptoms improved, and he was discharged from the hospital on the twenty-second day. In spite of the fact that a bruit was not heard and a lumbar puncture could not be made because of the danger of exciting further bleeding, it was concluded that the patient had a vascular lesion and that the attacks were due to bleeding as had been found in

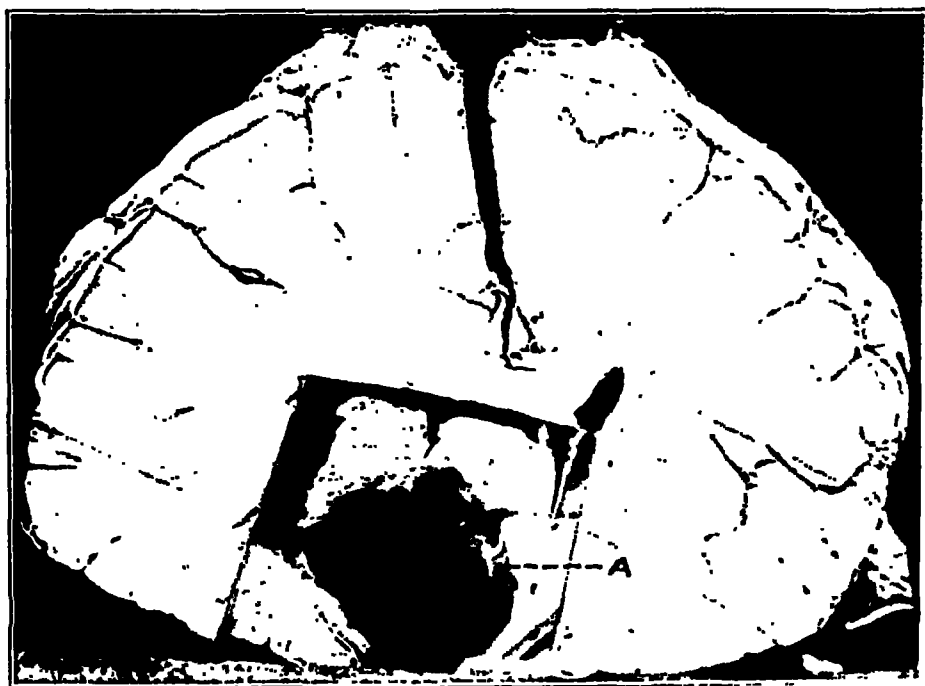


Fig. 12 (case 5).—Blood clot between the frontal lobes with the left anterior cerebral artery at *A*.



Fig. 13 (case 5).—Section taken from the area of blood clot in figure 12, showing the left anterior cerebral artery at *A* and the right anterior cerebral artery with an aneurysmal dilatation. The termination of the elastic tissue marking the extent of the arterial wall is shown at *B* and *C* below which the aneurysm extends.



Fig. 14 (case 6).—Above the sella turcica a calcified mass is seen.

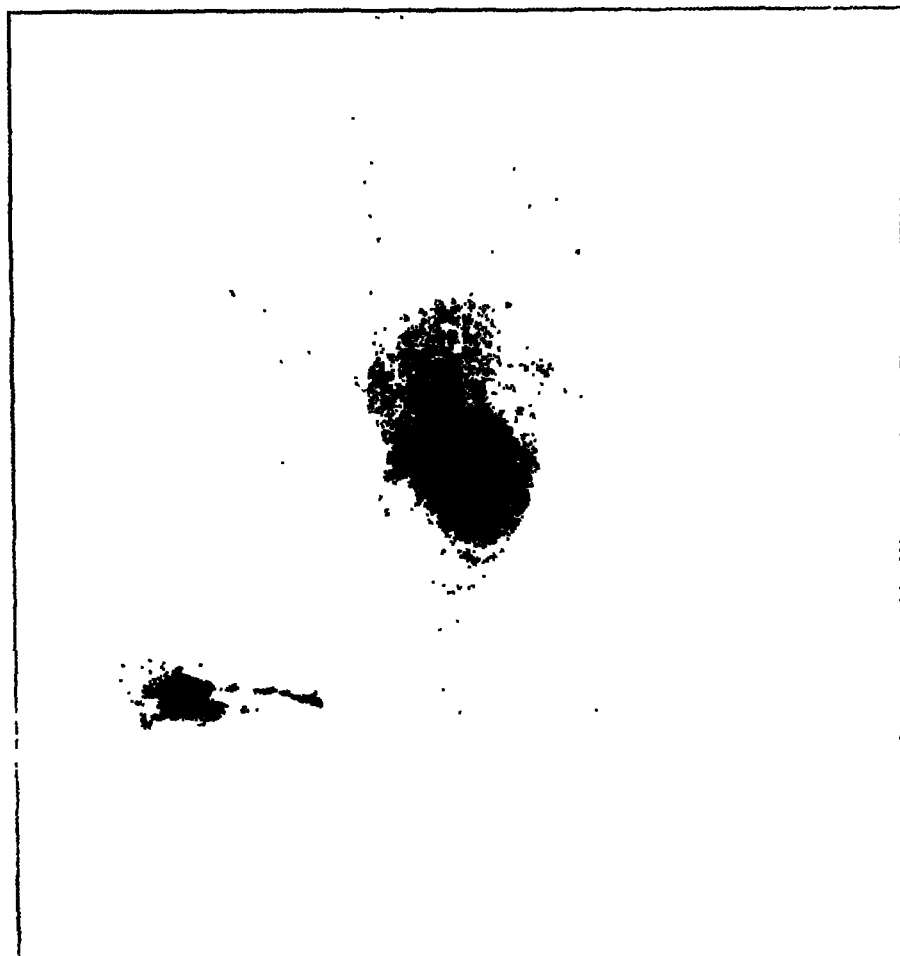




Fig. 16 (case 6).—Frontal section showing dilatated ventricles which were filled with fresh blood and the calcified mass at *A* shown in figures 14 and 15.

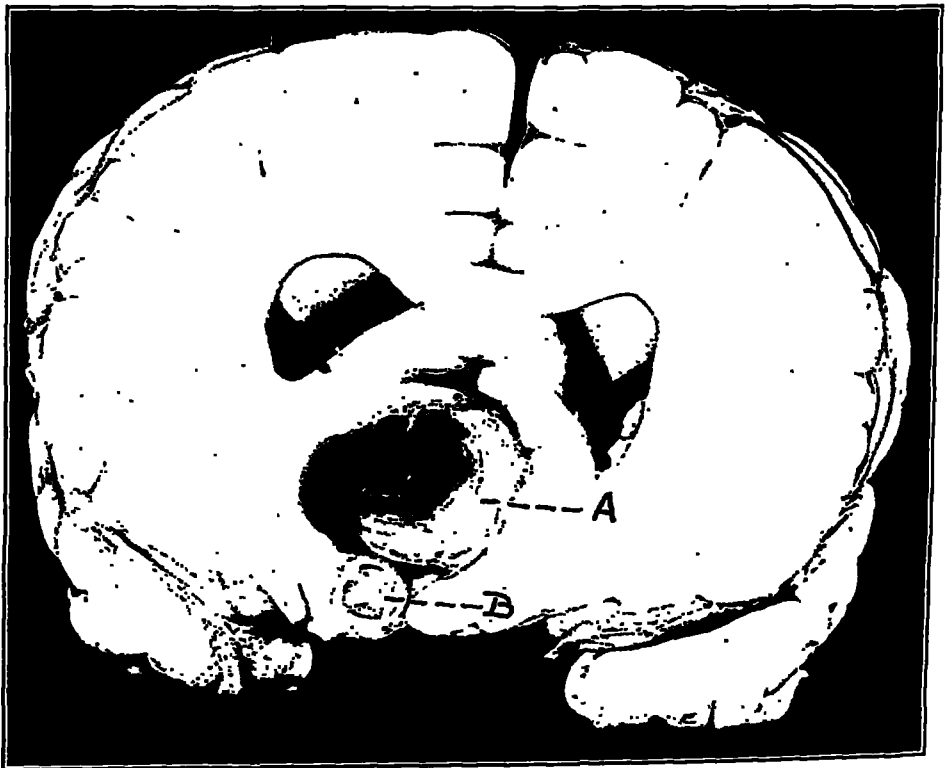


Fig. 17 (case 6).—Anterior cerebral aneurysm at *A* and calcified cyst at *B*.

death. In the wall of this mass beginning calcification was seen, and it is probable that this would have been similar to the large calcified mass if the patient had survived. In figure 18, the anterior cerebral artery at the caudal extremity of the aneurysm is shown. The thick wall of the aneurysm in this



Fig. 18 (case 6).—Anterior cerebral artery at its junction with the aneurysm shown at *A* in figure 17. The elastic tissue present from *B* to *C* is absent between the points of the arrows.

section was lacking in elastic tissue. Sections through the large sac as shown in figure 17 also demonstrated complete absence of elastic tissue.

CASE 7.—Clinical evidence of hemorrhage in the same area as shown in the three preceding cases in which the patients recovered following the initial attack.

Mrs. R. R., a woman, aged 34 years, while walking with her husband in the garden, suddenly exclaimed, "I have the funniest feeling in my head and it hurts. I am going into the house and lie down." I saw this patient three days later, when stupor, nausea and vomiting, marked bilateral edema of the disks with hemorrhages and abducens weakness were present. The cerebrospinal fluid, as obtained by lumbar puncture, was slightly bloody. Only a small amount of fluid was taken, and the puncture was not repeated because of the presence of choked disk and the possibility of exciting further bleeding. A cerebral bruit was not heard. The symptoms progressed for two days, when there was paralysis involving chiefly the muscles of the right side of the body. The paralysis and choking slowly disappeared, but there was some headache for two months. It is now eight months since the onset of the illness, and the patient is free from symptoms; however, there is grave danger of recurrence of the symptoms.

Until recent years, cerebral aneurysms have been mainly of pathologic interest. Five years ago, Dr. C. P. Symonds and Dr. Harvey Cushing³ called attention to the importance of clinical facts concerning these lesions. Slight hemorrhage with definite clinical manifestations usually precedes the large fatal hemorrhage in small cerebral aneurysms and must be considered in the differential diagnosis of obscure lesions of the brain.

The source of bleeding in infants is a matter of great importance. The bleeding is frequently due to tearing of the large dural sinuses, but in some cases it is probably due to tearing of the cortical veins as they enter the dura. The following case is included because of its course which typifies what happens when blood escapes into the cerebrospinal fluid and because of the specimen which shows the source of the blood.

CASE 8.—Small amount of blood in the cerebrospinal fluid following cerebral trauma; death in status epilepticus on the third day.

J. D., aged 6 months, was in excellent physical condition when left with a colored nurse. When the mother returned two hours later, the child was unconscious and the nurse did not give any indication of the cause. Twenty-four hours later the fontanel was tight, and there was a severe general convulsive seizure. Seizures occurred at short intervals until collapse eighty hours after the onset when the child died. Lumbar puncture during the third day revealed bloody cerebrospinal fluid.

Autopsy showed a moderate amount of blood mixed with the cerebrospinal fluid and a small blood clot over the left frontal cortex where a vein had been torn from the dura (fig. 19). The pia-arachnoid was thickened and the veins markedly dilated.

CASE 9.—Tumor of choroid plexus with hemorrhage into ventricle on the tenth day. The early date of bleeding created confusion with birth hemorrhage.

H. M., came under observation when 10 days old because of sudden increase in intracranial pressure, with vomiting, respiratory embarrassment and loss of consciousness. When the patient was examined about six hours after the onset

3. Symonds, C. P.: *Clinical Study of Intracranial Aneurysms, Part 1*, Guy's Hosp. Rep. 73:139 (April) 1923. Cushing, H.: *Clinical Study of Intracranial Aneurysms, Part II*, *ibid.* 73:159 (April) 1923.

of the symptoms, the fontanel was bulging and tense, and the cerebrospinal fluid contained a large amount of blood. The late onset of the symptoms without any indication of a hemorrhage during the first hours after birth and the quantity of fresh blood in the cerebrospinal fluid led to the suspicion of a lesion similar to that shown in case 1. Repeated lumbar punctures showed a gradual decrease in the amount of the blood, but the fluid remained yellow, and normal intracranial



Fig. 19 (case 8).—Specimen from an infant, aged 6 months, showing blood clot at the site of a torn cortical vein at point of attachment to dura. The clot is small and merely marks the point of escape of blood into the cerebrospinal fluid, which produced severe convulsive seizures and death.



Fig. 20 (case 9).—Tumor of the brain, the source of a large amount of blood in the cerebrospinal fluid on the tenth day after birth.

tension could not be maintained. At the age of 9 weeks the circumference of the head was 40 cm., the fontanel was large and the sutures were separated. With the view to determining the possible presence of hydrocephalus, air was introduced through a lumbar puncture needle. Only the right ventricle was filled

The right ventricle was then aspirated and air was injected, but again only the right ventricle was filled. A left osteoplastic bone flap was removed and a large solid tumor uncovered. The flap was replaced, and the child died twelve days later.

Examination of this tumor, shown in figure 20, proved to be a choroid plexus growth. The foramen of Monro was entirely occluded, and part of the left



Fig. 21 (case 10).—Cerebral meningeal reaction resulting from bloody cerebrospinal fluid due to injury of the spinal cord.

lateral ventricle of the forebrain which was not filled with tumor was greatly distended with blood-stained fluid.

CASE 10.—Cerebral irritation following bloody cerebrospinal fluid, extracranial source of blood with no likelihood of cranial injury.

The case of Baby B. is interesting because the injury at birth which was the source of blood was in the spinal cord, the blood reaching the cerebral sub-

arachnoid space in the same manner as in the experiments on dogs when the injections were made into the cisterna magna. The child was born after breech delivery and weighed 9 pounds (4.1 Kg.). From the beginning the condition was not satisfactory, and twelve hours later the temperature was 107 F. The fontanel was bulging slightly, and bloody cerebrospinal fluid was obtained on lumbar puncture. When 36 hours old, the child had two general convulsive seizures and died. The injury of the cord involved the eighth cervical and the first thoracic segments; from this point, blood had reached the cerebral cortex, producing marked clinical disturbance and the first stage of meningeal reaction shown in figure 21.

CASE 11.—*Chronic meningitis in which the clinical course and observations at autopsy suggest early bloody cerebrospinal fluid.*



Fig. 22 (case 11).—Arachnoid mesh at the fissure of Sylvius which before fixation in formaldehyde was greatly distended with cerebrospinal fluid.

M. B., aged 9 months, had had a normal birth and did well until the age of 2 months, when she was irritable and cried a great deal. The feeding was thought to be the cause, but frequent changes in the diet did not improve the condition. Vomiting was troublesome, and there was gradual increasing rigidity. When 6 months old, she had a severe general convulsion, following which the condition grew worse. When admitted to the hospital at the age of 8½ months, the child was undernourished and spastic, it had convulsive movements of the arms and legs, and the head was retracted. The cerebrospinal fluid was clear, with 2 cells per cubic millimeter. When the patient was admitted to the hospital, the temperature was 101.5 F., and it ranged between this and 107 F. until death two weeks later.



Fig. 23 (case 11).—A section from the base of the brain of an infant with clinical evidence of bloody cerebrospinal fluid showing meningeal thickening.

Autopsy revealed chronic meningeal thickening; the arachnoid at the sulci was opaque and edematous; in the sylvian fissure, it had the appearance of a veil-like sponge filled with fluid. In figure 22, the arachnoid mesh in which the fluid was held is shown; fixation of the tissue had caused the membrane to shrink below the level of the surrounding cortex in marked contrast to the distended membrane when seen in the fresh state. The meningeal thickening at the base of the brain is shown in figure 23.

My interest in the subject of bloody cerebrospinal fluid began during the summer of 1923, when the following case came under observation.

CASE 12.—Chronic meningitis, secondary to birth hemorrhage (clinical evidence). Gradual increase in the head and other indications of hydrocephalus.



Fig. 24 (case 12).—Chronic meningeal thickening with marked dilatation of the cortical veins.

Ventricle normal in size, a large amount of fluid over the cerebral cortex. Subtemporal decompression greatly diminished the meningeal thickening on the side drained, but had no influence on the undrained side.

P. C., aged 27 months, was apparently normal at birth. Jaundice was present on the second day and lasted for some weeks. Vomiting was troublesome on the fifteenth day and had continued irregularly, making it difficult to keep up body nourishment. At the time of the examination, the child weighed 22 pounds (10 Kg.). The appearance of the head indicated hydrocephalus, the fontanel was large, circumference 48 cm., thin, fine hair was present over the scalp, and there was internal squint of both eyes. Air injected into the ventricles showed both ventricles to be of normal size, but a large amount of air escaped over the cortex. A right subtemporal decompression revealed large cortical veins which were matted together, especially in the sylvian fissure. The arachnoid was thickened and

opaque. There was a large amount of cerebrospinal fluid over the cortex. A drain was inserted, and following the operation there was free drainage of cerebrospinal fluid which continued even after removal of the drain. The child died of pneumonia twenty-two days after the operation. The particular interest in this case is found in the examination of the brain, first because of the undilated ventricles in a child with a large head and other indications of hydrocephalus; second, because of the difference in the meninges and meningeal vessels on the drained and undrained sides of the brain. Grossly, the drained side was lighter in color than the undrained side, which was dark and cyanotic, suggesting a venous stasis. The veins of the undrained side were large, and small tributaries were plainly visible (fig. 24), while on the drained side (fig. 25) the veins were smaller, and the tributaries were not seen. Microscopically, the pia-arachnoid was much



Fig. 25 (case 12).—The opposite side of the brain shown in figure 24. When explored twenty-two days before death this hemisphere had the same appearance as that shown in figure 24. Free drainage of cerebrospinal fluid during the interval between operation and death greatly improved the drained side, but seemed to have had no influence on the undrained side.

thickened, the walls of the vessels were heavy and they were dilated on the undrained side. The difference in the membrane at the top of a sulcus is shown in figures 26 and 27. Deep in the sulci, the changes were marked. In figure 28, taken from the undrained side, there is a large amount of fibrous tissue and the vessel walls are thick in sharp contrast to the more delicate arrangement of these structures in figure 29, taken from a sulcus of the drained side. The lesions shown in the examination of the meninges of this brain were like those found in the young dogs following the injection of blood in the cerebrospinal fluid, and were similar to those found in verified cases of bloody cerebrospinal fluid in infants which in some instances presented the same clinical picture so that it

seems fair to assume that this child had a hemorrhage, though lumbar puncture was not performed early.

In its most simple form, bloody cerebrospinal fluid is seen in a type of hemorrhage in the new-born. Such cases show a disturbance ranging from twitching to general convulsive seizures during the first few days immediately following delivery. The story of hemorrhage in the



Fig. 26 (case 12).—The dilated vessels and thickened arachnoid mesh on the undrained side.

new-born has been told many times and need not be repeated here, so that only a few cases illustrating types of cases and methods of treatment are included.

CASE 13.—*Small amount of blood in the cerebrospinal fluid during birth, with mild cerebral disturbance; entirely controlled by repeated lumbar punctures.*

Baby J. F. B., a breech delivery, was apparently normal until about 24 hours of age, when he became limp and cyanosed and had attacks of twitching involving the whole body. These twitchings occurred at intervals of from two to three hours. A lumbar puncture was made on the third day, and yellow cerebrospinal fluid was obtained. The following day there was no improvement in the condition, and a second lumbar puncture was performed. The fluid obtained was more



Fig. 27 (case 12).—Pia-arachnoid on the crest of a gyrus near a sulcus, showing the more delicate arachnoid mesh than in figure 26.

deeply tinged than that withdrawn at the first puncture. During the observation, there were constant jerkings of the entire body—more marked in the left arm. After the second puncture, there was marked improvement in the condition, with milder attacks occurring at longer intervals. On the fifth day, lumbar puncture revealed a more deeply stained cerebrospinal fluid. The fluid flowed without any evidence of pressure. Attacks were not noted after the fifth day. Several

punctures were made during the latter period of the stay in the hospital, and the fluid gradually returned to a normal color.

This child is now entirely normal at the age of 27 months.

With a history such as that obtained in this case, lumbar puncture is always recommended. Care must be taken in doing the puncture to avoid trauma, particularly when done in the first forty-eight hours, and for this reason, I practice giving a few drops of chloroform and use a small Luer hypodermic needle. When bloody fluid is obtained, the child



Fig. 28 (case 12).—Pia-arachnoid deep in a sulcus on the undrained side showing fibrous tissue and cell infiltration.

is generally better after the first or second puncture, but I make repeated punctures even in the absence of symptoms until the fluid is entirely clear. The intervals between punctures depend on the severity of the symptoms (being shorter in severe cases) and the amount of blood present. It is recognized that a new-born child with some blood in the cerebrospinal fluid will recover spontaneously, but when the blood has produced symptoms, the normal recuperative powers should be aided by repeated punctures.

Fortunately, the greater number of hemorrhages at birth, excluding those desperate cases in which there are massive hemorrhages, fall into this group.

Major operative procedures are recommended only in selected cases because of the high mortality which discourages all effort, resulting in the attitude, still too frequently encountered, that a child with a hemorrhage is so likely to be a defective that it is better for it to go

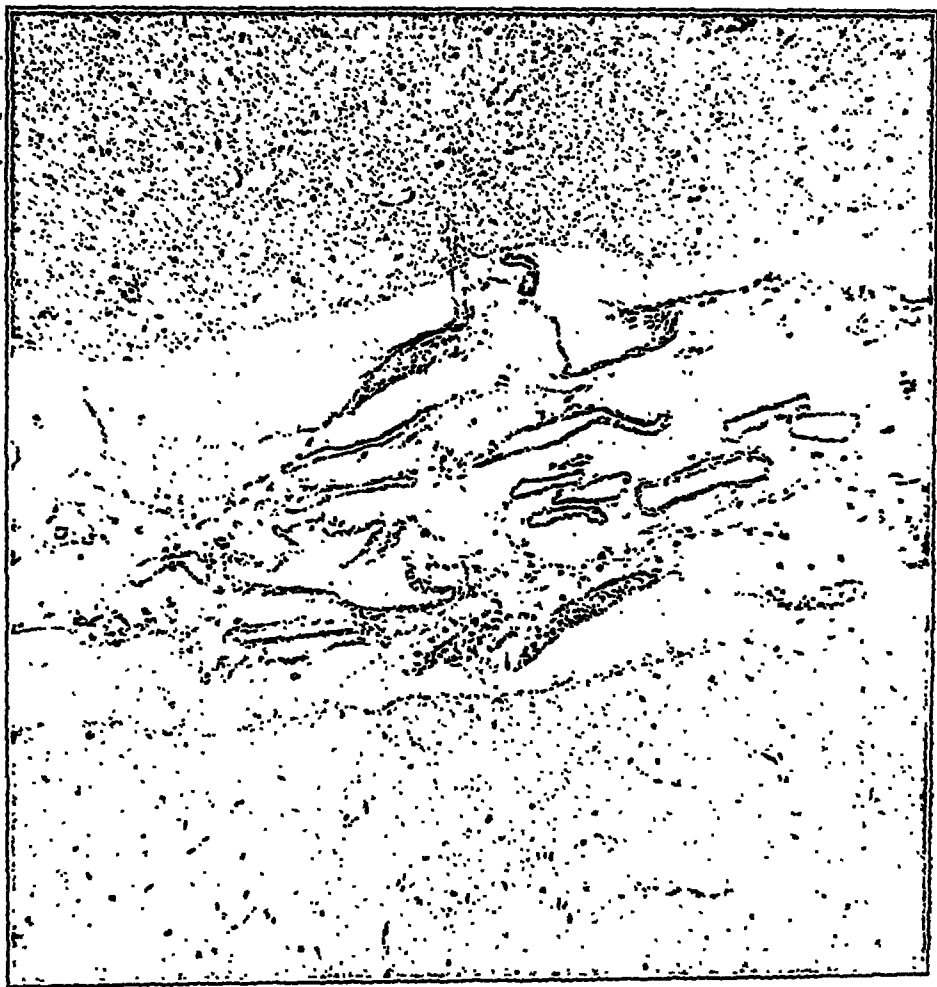


Fig. 29 (case 12).—Pia-arachnoid deep in a sulcus on the drained side in marked contrast to that shown in figure 28 corresponding to the gross changes in figures 24 and 25.

untreated with the hope that it will succumb. This is unfair in that it does not give the child a chance, and especially because many of the untreated survive with a poor chance for normal cerebral development. A good example of this was seen in a child who had had severe convulsions immediately after birth. The diagnosis of cerebral hemorrhage was made, and there was a stormy course for a month, during which time little hope of recovery was maintained. After a few weeks the

child had apparently recovered, but at the age of $3\frac{1}{2}$ years, a general convulsive seizure was followed by other seizures at intervals of a few months.

General muscle rigidity is a prominent sign in neglected cases and usually starts when the acute signs of cerebral irritation cease.

CASE 14.—Cerebral irritation when a few days old. Muscular rigidity at 1 month, which increased until treatment, lumbar puncture, was instituted at age of 2 months. Condition satisfactory when child was 6 months old.

Baby P. Z., when a few days old had had a seizure, with marked cyanosis. When the child was 2 weeks old the mother noticed postcervical rigidity. At the age of 1 month there was general rigidity, and the head was drawn back to such an extent that the child could not lie in the dorsal position and could be raised from a lying to a sitting position by lifting the head (fig. 30). Because the eyes were rolled upward and did not follow an object, the mother also feared he could not see. Repeated lumbar punctures, fourteen in all, over a period of four months, were followed by satisfactory disappearance of the rigidity.



Fig. 30 (case 14).—The postcervical rigidity permitted the child to be raised to a sitting position by lifting the head (illustration taken from a moving picture film).

From this time, the mental and physical condition of the child did not cause concern. The photograph (fig. 31) was made when the child was 1 year of age to show normal muscle control.

The history of cerebral irritation during the first few days of life and the fact that improvement follows lumbar punctures differentiates these patients from the large group of children with spasticity resulting from developmental defects.

One child came under observation at the age of 9 years. This child, with her twin had had a normal birth, and at the age of 4 weeks was examined by the pediatrician, who told the mother that the patient was the better of the twins because of her ability to hold her head and spine erect. This probably indicated the early rigidity of a chronic meningitis; the mental and physical development of the patient, not so good as that

of the other twin, merged into a state of epilepsy at the age of 9 years. The head of the child had the appearance of a slight degree of hydrocephalus, and this fact was borne out by the roentgenogram of the air filled ventricles.

In a few cases, lumbar puncture will not control the symptoms, and a more complete and thorough drainage must be established through a decompression or osteoplastic flap.

CASE 15.—Cerebral irritation at age of 1 week. After repeated lumbar punctures, all symptoms disappeared, except muscular rigidity, which improved during a period of subtemporal drainage but returned when drainage ceased. An osteoplastic bone flap followed by drainage entirely relieved the condition.



Fig. 31 (case 14).—Normal muscle control when a little more than 1 year old (illustration taken from a moving picture film).

E. S., had had a convulsion on the seventh day after birth, and there was bulging of the fontanel. Lumbar puncture revealed blood-stained cerebrospinal fluid, diminished the bulging of the fontanel, and the convulsions ceased. Repeated punctures, six in all, until the age of 6 weeks, improved only temporarily the state of rigidity and the tension of the fontanel. At this stage, a more radical procedure was deemed necessary; an opening was made in the right subtemporal region, and a small rubber tissue drain was inserted. As long as drainage of cerebrospinal fluid continued, the condition of the child was satisfactory, but soon after the drain was removed, on the ninth day after operation, the tension and rigidity returned. The mother expressed anxiety over the condition of the child as compared with her two other normal children at this age. On the seventy-second day after birth, a right osteoplastic bone flap was done with the

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hope of draining more thoroughly the subarachnoid space. When the pia-arachnoid overlying the hemisphere was exposed, a low grade meningitis similar to that seen in the dogs was found. Drains were inserted over the cortex, and the dura was closed loosely. The rigidity gradually diminished and disappeared. The fear of the mother that the child would be backward, entirely subsided as normal mental and physical development (fig. 32) progressed throughout the first months after the operation. The child is now 4 years old and is quite like her brother and sister.



Fig. 32 (case 15).—Patient at the age of about 16 months showing an active, alert child.

Six of the twenty-six puppies injected had a rather marked degree of ventricle dilatation associated with chronic meningeal thickening and cortical scarring. The dilatation did not progress to an extreme degree and was associated with an excess of fluid over the cortex, which leads to the belief that the cerebrospinal fluid blocking was due to interference of absorption rather than to a blocking at the basal foraminae.

The two following cases in which the patients had slight enlargement of the ventricle and a large amount of fluid over the cortex with clinical evidence of hydrocephalus are of this type, although the cerebrospinal fluid blockage is different from that seen in case 1.

CASE 16.—Cerebral trauma at the age of 2 months. Indefinite cerebral symptoms with gradual enlargement of the head until 8 months of age when examination showed slight enlargement of the ventricles and a large amount of fluid over the cerebral cortex.



Fig. 33 (case 16).—Large amount of air over the cerebral cortex with only slight dilatation of the cerebral ventricles. The air was introduced through a lumbar puncture needle after the withdrawal of a large amount of fluid.

Baby W. W., fell from his crib at the age of 2 months. Little attention was paid to the injury, but during the following weeks the child was listless and inactive. At the age of 8 months, he was unable to hold up his head. When examined by me at the age of 9 months, the circumference of the head was 45.5 cm., the sutures were separated, and the fontanel was large and tense, giving the child a typical hydrocephalic appearance. A large amount of cerebrospinal fluid was withdrawn through a lumbar puncture needle, and air was injected (figs. 33 and 34). The illustrations show a large amount of air over the cerebral cortex with only slight dilatation of the ventricles. Repeated lumbar punctures failed to control the symptoms. Because of the long duration and the

advanced stage of the condition, so little was promised the parents that they declined operation. The child is now 2½ years old and is entirely helpless.

CASE 17.—Small amount of blood in the cerebrospinal fluid at birth. Early cerebral irritative symptoms and during the third month evidence of hydrocephalus. Ventricles only slightly enlarged but a large amount of fluid over the cerebral cortex. Condition corrected by osteoplastic bone flap with free drainage of cerebrospinal fluid on one side and decompression with free drainage on the other side.

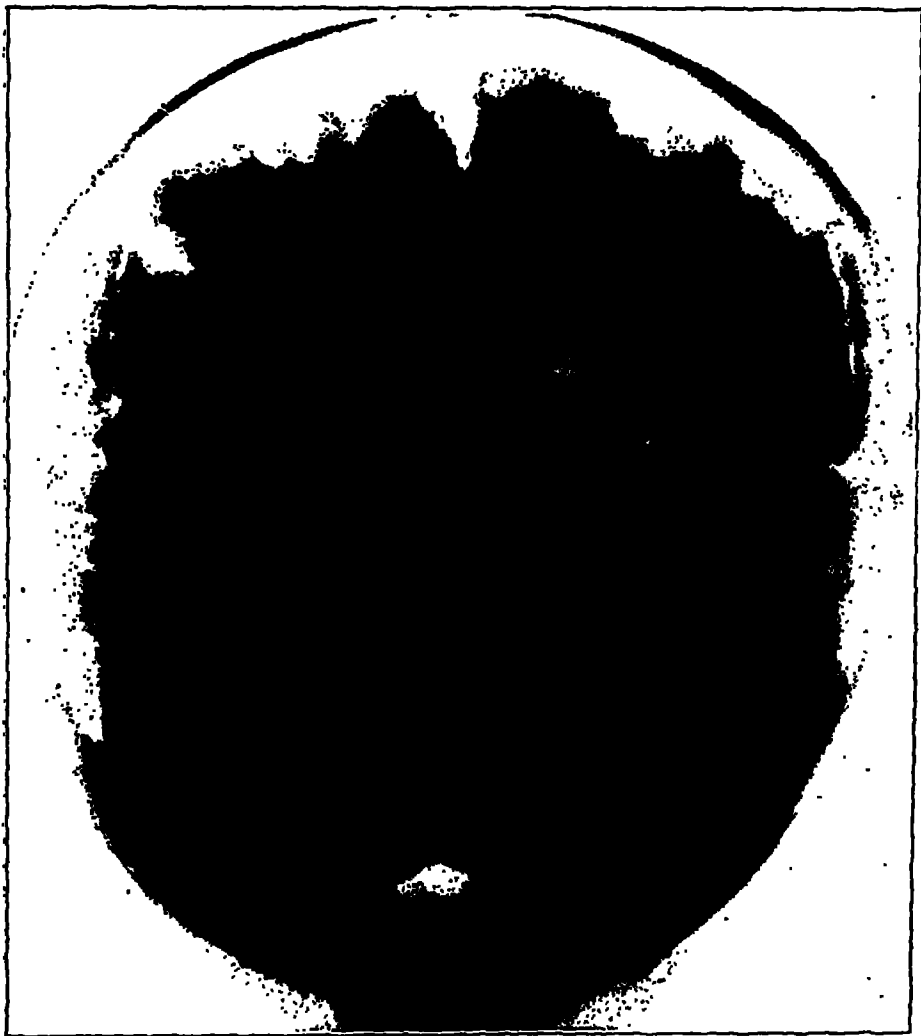


Fig. 34 (case 16).—Anteroposterior view also showing a large amount of air over the cerebral cortex with wide sulci.

Baby V. D., was delivered with high forceps after slow labor. Immediately after delivery, the condition was satisfactory. Later in the day, there was slight twitching of the hands and feet with some cyanosis. For the next forty-eight hours the child cried a great deal and refused to nurse, and its temperature ranged as high as 103 F. Lumbar puncture on the third day revealed cerebrospinal fluid with a pale yellow tinge. Because of the mild degree of twitching and the fact that the fluid was yellow on the third day, a favorable prognosis was given, as

it was believed the small amount of blood would be absorbed. Another puncture was advised to check the condition of the cerebrospinal fluid before the mother and the baby were discharged from the hospital. On the seventeenth day after birth, I examined the child again; the circumference of the head was 39 cm., the veins of the scalp were dilated, especially those from the bregma over the frontal region, the fontanel was tense, and the sutures were separated. Lumbar puncture revealed a more deeply yellow-tinged cerebrospinal fluid than at the time of the puncture two weeks previously. Three days later, the circumference of the head had increased 5 mm., and the cerebrospinal fluid pressure was 180 mm. of water. The appearance of the child was now definitely that of one with a



Fig. 35 (case 17).—Air injected through a lumbar puncture needle after the withdrawal of cerebrospinal fluid is shown in the wide sulci and over the cortex. The ventricles not shown in the print were slightly dilated.

beginning hydrocephalus, and it was determined to perform punctures at short intervals. Twelve additional punctures at intervals of from two to five days were made. When the child was 7 weeks old, air was introduced through a lumbar puncture needle, and the roentgenogram showed wide sulci, an abnormally large space between the cortex and the dura and a slight enlargement of the ventricles indicating an excessive amount of cerebrospinal fluid (fig. 35). At the age of 9 weeks, in spite of the lumbar punctures, the circumference of the head was 42 cm., the fontanel was larger, the sutures were separated, the

veins of the scalp dilated, and the head was heavy, requiring support when the child was picked up.

At this time, an osteoplastic bone flap was made uncovering a large part of the right cerebral hemisphere. The pia-arachnoid was definitely thickened. The cortical veins were engorged, and the arachnoid over the sylvian fissure and the sulci was literally distended with fluid. When the membrane over the sylvian fissure was punctured, fluid slowly escaped as though seeping from a mesh. The wound was closed with a drain. For several days after the operation, there was free drainage of cerebrospinal fluid. Three weeks after operation, the circumference of the head was 41.5 cm., the fontanel was soft, scalp veins were not overfilled, and the child had regained some control of the muscles of the neck but was still unable to hold the head erect. The condition continued to improve for several weeks, when the tension was again increased and the head began to enlarge. Frequent lumbar punctures were tried, but failed to control the con-



Fig. 36 (case 17).—Photograph of patient at the age of 13 months. The head is larger than normal, but the sutures are closed, and there is no evidence of increased intracranial tension.

dition, and at the age of 19 weeks an opening was made in the left temporal region and drains were inserted. From this time on, the fontanel gradually decreased in size and the circumference increased only at the normal rate. The condition of the child at the age of 13 months is shown in figures 36 and 37. Except for slight enlargement of the head, the physical and mental condition is entirely normal.

The clinical course in this case, different from that of the other groups described, typifies what happens infrequently, but which I believe is nevertheless a definite clinical entity. Through the irritating effects of the blood in the cerebrospinal fluid, there is interference with the

absorption of the fluid. Puncture of the dura as by lumbar puncture in the milder cases or by an extensive opening as a bone flap in the more severe types unblocks at some point, and absorption is reestablished.

That the opening of the dura has an influence on this type of case was first brought to my attention in a child born after a prolonged and difficult labor, who was normal for a period of two weeks, after which



Fig. 37 (case 17).—Lateral view of the head at the age of 13 months.

there was rapid enlargement of the head. It was thought that there was a blood clot over the cerebral cortex, and several small openings were made through the skull and dura. A clot was not found, and the wounds were closed tightly. From the time of the operation, the head ceased to enlarge. An explanation of this was not had at the time, but I now believe that the mere opening of the dura helped rid

the subarachnoid space of the irritating cerebrospinal fluid. This child is now 13 years of age, has always been backward, and since the age of 5 years, has had convulsive seizures. Early complete subarachnoid drainage, would perhaps, have given this child a much better chance.

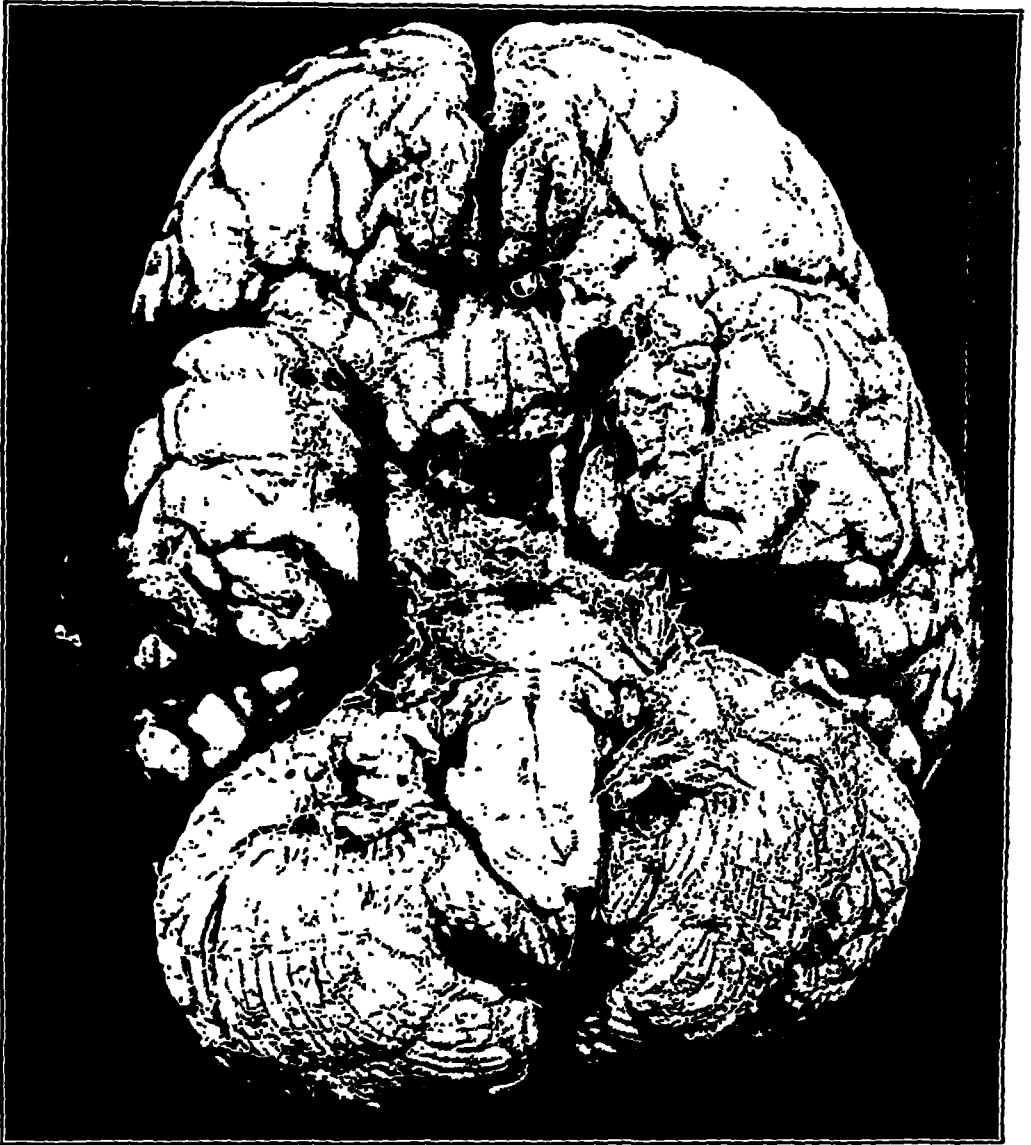


Fig. 38 (case 18).—Meningeal thickening twenty days after cerebral trauma with bloody cerebrospinal fluid.

In 1903, Dr. William G. Spiller⁴ called attention to the importance of cases of cerebral trauma without displacement of bone in which a blood clot, even though small, is present, and in spite of the early disap-

4. Spiller, W. G.: *Traumatic Lesions of the Brain in Their Relation to Operation*, *Internat. Clin.* 4:102, 1923.



Fig. 39 (case 18).—Section of the meninges from the base showing meningeal thickening and cell infiltration.

pearance of symptoms of compression, the patient is in danger of becoming epileptic or developing traumatic insanity.

In 1904, Dr. Adolf Meyer⁵ in his discussion of mental patients who had previously had a cerebral trauma remarked: "Whether the cranium is fractured or not means relatively little. It would seem, however, that for chances concerning life, a relatively extensive destruction of the skull is rather more favorable than otherwise."

In the light of my experimental work the drainage of cerebrospinal fluid seems to be of paramount importance, and I am inclined to feel that the danger of immediate and late symptoms is lessened in the compound cases in which the dura is opened allowing a free escape of blood and cerebrospinal fluid.

Dr. Harvey Cushing,⁶ in his paper in 1907, calls attention to the advisability of decompression and drainage. This marks the beginning of a type of cranial surgery which has proved very useful. Confusion in the selection of patients for operation occurs because of failure of surgeons to consider carefully the underlying lesion in attempting to determine whether the patient should or should not be treated by decompression. For instance, in some clinics, an attempt has been made to settle the question by operating on a given number of consecutive "fractured skulls" and comparing them with a second series, none of which were subjected to operation. The outcome of these discussions has resulted in the conviction that there is a type of case in which the patient may recover spontaneously, but the recovery can be speeded and a more simple postoperative course can be assured by drainage of cerebrospinal fluid. It has further been recognized that in many of these cases the bloody cerebrospinal fluid can be drained through repeated lumbar punctures, thus avoiding the more radical procedure of decompression and drainage. Here again the pendulum may swing too far, and care must be taken not to overlook the case in which lumbar puncture will not suffice and a decompression or even a bone flap is required.

The importance of bloody cerebrospinal fluid as a result of injuries without displacement of bone is shown in the following fatal case in which the symptoms immediately after the injury were slight. During the second week, meningeal irritative signs gradually developed to a serious stage, and the patient died during the third week in spite of lumbar puncture and late decompression.

CASE 18.—Late appearance of symptoms following the escape of blood in the cerebrospinal fluid. Decompression delayed until the sixteenth day after the

5. Meyer, A.: The Anatomical Facts and Clinical Varieties of Traumatic Insanity, *Am. J. Insan.* 60:373, 1904.

6. Cushing, A.: A Discussion of some Immediate and some Remote Consequences of Cranial Injuries, Based on Three Clinical Histories Which Illustrate the Extradural, Subcortical, and Intermenigeal Types of Intracranial Hemorrhage, *New York M. J.* 85:214, 1907.

accident accomplished nothing. Section of the meninges showed marked meningeal reaction.

G. G., a man, aged 35, was thrown from an automobile and struck his head. He went to his home, and his condition did not cause any concern until the end of the first week, when there was headache and mental confusion with slight elevation in temperature. He was treated at home for several days, during which time the symptoms increased. When the patient was admitted to the hospital fourteen days after the accident, the pulse rate was 60 per minute, there was postcervical rigidity, a positive Kernig sign, some delirium, severe headache and beginning choking of the disks. Lumbar puncture showed yellow-tinged cerebrospinal fluid. Following the puncture, the patient was more comfortable. A second lumbar puncture was made after an interval of six hours, and a third, twenty-four hours later. The symptoms increased, and a right subtemporal decompression was performed forty-eight hours after admission, at which time the patient presented the appearance of one suffering from advanced meningitis. When the dura was opened, there was bulging of the cortex and only a small amount of cerebrospinal fluid escaped, indicating that the condition had reached the stage of cerebral edema. The pia-arachnoid was opaque, but there was no evidence of exudate. Drains were inserted over the cortex. Following the operation, there was scant drainage of cerebrospinal fluid, and the condition grew worse until death four days later. Autopsy revealed a film of blood mixed with cerebrospinal fluid throughout the subarachnoid space. The meninges at the base were thickened (fig. 38) and blood-stained. A section of the meninges from this area (fig. 39) showed the reaction.

In this case, the disturbance at the time of admission to the hospital is now believed to have been due to edema of the brain which, no doubt, followed a stage in which there was an excess of fluid in the subarachnoid space. The period for lumbar puncture had passed, and a more radical procedure for complete drainage was indicated.

In the following case, lumbar puncture was not made, as there was evidence of "medullary disturbance." On the fourth day, a convulsive seizure occurred, and because of the serious condition following it, a right subtemporal decompression was performed.

CASE 19.—Cerebral trauma with a general convulsive seizure and complete loss of consciousness on the fourth day.

J. G. N., a married woman, aged 40, was injured in an automobile accident, receiving a blow in the right frontal region. She was admitted to the hospital one hour later, when there was some bleeding from the nose and right external auditory canal; the blood was not mixed with the cerebrospinal fluid. In the beginning she was unconscious; this condition improved, but mental confusion continued. In spite of evidence of "medullary disturbance" with marked increase in the deep reflexes, clonus and a bilateral Babinski sign, the condition did not seem alarming until the afternoon of the fourth day, when she had a convulsive seizure with cyanosis, a severe drop in the blood pressure, pulse and respiratory rate, the latter reaching 10 per minute. Following the seizure, there was complete loss of consciousness for four hours, at which time a right subtemporal decompression and free drainage of cerebrospinal fluid were accomplished. Following the operation there was prompt recovery, and the patient was discharged on the twelfth day, at which time there was some blurring of vision and slight mental confusion. When examined recently two and a half years after the accident, the patient was normal.

The sudden onset of symptoms in a man four days after an accident is shown in the following patient:

CASE 20.—Cerebral irritation with bloody fluid four days after trauma promptly relieved by lumbar puncture.

J. S., a man, aged 34, was admitted to the hospital immediately after an injury in the right frontal region of the head. There was little headache, and the temperature ranged from normal to 100 and the pulse rate from 70 to 100 per minute for the first four days. During the evening of the fourth day, the patient complained of severe neuralgia-like headache; he vomited, and the temperature registered 97 F. with a fall in pulse rate to 60 per minute. Lumbar puncture revealed bloody cerebrospinal fluid. Later, lumbar puncture showed the cerebrospinal fluid gradually returning to normal, and all symptoms disappeared.

The symptoms in this patient were due to a gradually increasing meningitis. It is unwise to disturb a patient who is apparently doing well, but an early lumbar puncture would have prevented the severe reaction in this case. One year after the accident this patient had indefinite symptoms, such as headache and dizziness of a mild degree.

The late appearance of signs and symptoms is shown in the following case:

CASE 21.—Cerebral trauma with bloody cerebrospinal fluid. Gradually increasing symptoms for two weeks; gradual disappearance of symptoms following repeated lumbar puncture.

W. C., a man, aged 20, received a severe blow over the right frontal region of the head while playing football. After a few moments he continued playing, and in spite of a slight headache, worked the following day and attended a dance during the evening. He complained slightly, and forty-eight hours after the injury consulted his family physician because of mild headache and occasional vomiting. Two weeks after the date of the injury, I saw him because the pulse rate was ranging from 48 to 52 per minute. He was rather dull when left alone, but when stimulated, would talk and seemed entirely normal. He said there was no real headache, but a feeling of tightness and some tenderness of the scalp. The examination showed a rather listless youth with speech distinct but slow. The disks showed definite changes from the normal, with a mild degree of choking. Three hours after the puncture, the patient said he felt different. The dull feeling in the head was gone, and he was more alert. Lumbar puncture twenty-four hours later showed the same yellow fluid. Two weeks after the first puncture, the fluid was almost entirely clear. Twenty-six days after the first puncture, because of nervousness, another puncture was made and the fluid was colorless. The patient did not complain of headache, and returned to his work.

CASE 22.—Cerebral trauma with symptoms two weeks later, but patient not treated until one month after the accident. Well marked meningeal reaction with evidence of increased intracranial pressure, relieved by decompression and drainage.

R. S., a boy, aged 12, fell from a fence and struck his head in the left parietal region. There was nausea and vomiting and some headache for two days. After that time he seemed normal, but later developed an internal squint of the right eye and complained of photophobia. He played normally for two weeks, when there was some drowsiness, and he was inactive for the greater part of the next two weeks. When examined four weeks after the accident, there was marked choking of the disk, paralysis of the right external rectus and stupor, but he could

be aroused to carry out simple commands. The pulse rate was 60 per minute, the leukocytes numbered 11,000, and a suggestive Kernig sign was present. The roentgenogram showed a linear fracture of the right parietal region. A right subtemporal decompression was performed, and drains were inserted. The dura was tense, and when opened there was free drainage of cerebrospinal fluid. The following day, the external rectus muscle was less weak. All symptoms gradually disappeared during a period of three weeks, when the patient was discharged.

CASE 23.—*Cerebral trauma with delay of serious symptoms for seven weeks. Late appearance of convulsions and partial hemiplegia at first led to the diagnosis of apoplexy. Because of history of trauma, decompression with drainage was done.*

F. S., a man, aged 55, fell on his head while climbing an ice-covered wooden fence. He was at first dazed, but walked home. Three weeks later, he had vague symptoms for which he consulted a physician. Seven weeks after the accident, he returned home after attending church, walked upstairs to retire for the night and had a convulsive seizure, after which there was headache and vomiting, slight weakness of the right side of the face and of the arm and mental confusion. The symptoms continued, and I first saw him four days later. Examination at that time revealed the patient in stupor; the pulse rate was slower than normal, there was a mild choking of the disks and slight weakness of the right side of the face and of the right arm. With the history of the sudden onset four days before, the diagnosis of cerebral hemorrhage was made. In discussing the case with the patient's wife following the consultation, she remarked that the patient had never been the same since he fell over the fence. This was the first mention of the accident, which, because of the interval of seven weeks, had not been thought to have any connection with the present condition, and was not mentioned by the other members of the family who had originally given the history. Careful questioning revealed that the patient had had vague symptoms and had consulted a physician for slight headache three weeks after the accident. It was then concluded that the symptoms were, perhaps, due to the accident, and exploration was advised. During the period of twenty-four hours in the hospital before the operation, the temperature ranged from 100 to 101 F., and the pulse rate from 45 to 65 per minute. There was beginning choking of the disks, weakness of the muscles of the right side of the body and stupor. Decompression was performed and an opaque arachnoid with distention of the cortical vessels was seen. A drain was placed beneath the dura and the wound was closed. Following the operation, there was a gradual falling of the temperature, which reached normal on the eighth day after admission. All symptoms improved, and the patient was discharged from the hospital on the thirty-third day. Ten years have passed since the operation, and the patient is living and well.

Just what part syphilis plays in spontaneous cortical hemorrhages with extravasation of blood into the cerebrospinal fluid has been variously stated.

CASE 24.—*Cerebral syphilis with a sudden hemorrhage into the cerebrospinal fluid followed by severe pain and delirium. Gradual improvement of symptoms for five days. Lumbar puncture on the fifth day showed yellow fluid. Rapid improvement following lumbar puncture.*

G. J., a married man, aged 37, while driving his car on April 27, 1923, was suddenly seized with severe headache and vomiting. He was taken to the office of a physician in a state of collapse. For one week following the onset of symptoms, he was wildly delirious. There was elevation in temperature, and the pulse rate was rapid. He was admitted to the hospital five days after the attack,

complaining of headache and pain in the extremities. Lumbar puncture made the next day revealed slightly bloody cerebrospinal fluid; another a week later showed clear yellow cerebrospinal fluid. The patient was discharged from the hospital eleven days after admission, the stupor following his delirium having cleared up. The Wassermann reaction of the blood and cerebrospinal fluid was positive, and the patient was treated for syphilis. It is now almost five years since his discharge from the hospital, and there has not been any recurrence of the symptoms. The symptoms in this type of case are due to meningeal irritation. The fact that this patient had syphilis and had refused thorough treatment was known to his physician; he, therefore, attributed the mental upset to this, and was planning to have the patient committed to an institution. As the condition improved after five days, the patient was admitted to a general hospital, where it was decided the mental condition was due to the blood in the cerebrospinal fluid.

Arteriosclerosis and hypertension play an important rôle, and care must be taken to differentiate cases in which the symptoms are due to escape of blood into the cerebrospinal fluid from those due to a hopeless subcortical clot. The first intimation of the hopeful type is found when the patient shows evidence of meningeal irritation ranging from severe headache and postcervical pain to rigidity and convulsive seizures with elevations in temperature and pulse rate. In either type there must be some blood in the cerebrospinal fluid; but a lumbar puncture with the withdrawal of even a small amount of fluid will cause improvement in patients with the simple type and will have a bad influence if any on patients with subcortical clot.

CASE 25.—Cerebral arteriosclerosis with bloody cerebrospinal fluid and severe cerebral irritative symptoms which were relieved by repeated lumbar punctures.

J. H. S., a married man, aged 54, after hurriedly driving his car, became slightly confused mentally and thick in his speech. There was a slowly increasing stupor, which was never deep. Two hours after the onset, the patient had a general convulsive seizure; during the next ten hours, he had three more, at which time there was slight weakness of the right side of the face and of the right arm. The blood pressure was 200 systolic and 130 diastolic and later dropped to 190 systolic and 90 diastolic. When I examined the patient the first time, at 4 p. m., the following day, twenty hours after the onset of the trouble, there was partial aphasia and slight weakness of the right arm and of the right side of the face, and the reflexes were greater in the right than in the left upper extremity. There was stupor and mental confusion. The patient seemed to be uncomfortable because of headache. On lumbar puncture, bloody cerebrospinal fluid was withdrawn. Following the puncture, the patient was more comfortable. Repeated punctures were made until the fluid was clear one week after the onset, and the patient gradually improved, though the aphasia never entirely cleared up. The patient is still living, two and one half years later, the blood pressure has remained high, and he now presents the usual picture of cerebral arteriosclerosis.

CASE 26.—Bloody cerebrospinal fluid perhaps due to rupture of an arteriosclerotic cerebral vessel. On admission of patient to hospital one week after sudden onset, the signs and symptoms suggested tumor of the brain. Repeated lumbar punctures followed by disappearance of all signs and symptoms.

Mrs. C. G., aged 56, was suddenly seized with severe pain in the head. Within twenty-four hours the patient was in coma which lasted for several hours. Severe headache with paroxysmal attacks of agonizing pain and loss of consciousness

occurred several times daily. When admitted to the hospital one week after the onset, she showed bilateral choked disks, bilateral abducens weakness and slight weakness of the left side of the body, including the face. There was postcervical rigidity and positive Kernig sign. Dizziness was troublesome, especially when the position was changed. The diagnosis of cerebellar tumor was made, but because, of the sudden onset, postcervical rigidity, positive Kernig sign, and slight elevation in temperature and increased pulse rate, the immediate cause of the symptoms was believed to be due to the escape of blood in the cerebrospinal fluid. A lumbar puncture was made, and bloody cerebrospinal fluid was obtained. The condition was followed by immediate temporary improvement in the symptoms. Repeated lumbar punctures, nine in all, brought about a subsidence of symptoms, though the disturbance of the eye movements persisted for three months. Convalescence was slow, but the patient is living and well and free from symptoms with a blood pressure of 160 fifteen months after the illness.

Lumbar puncture in the presence of choked disk due to tumor is an extremely dangerous procedure; on the other hand, when there is an excess of cerebrospinal fluid, a lumbar puncture is not dangerous but offers relief. In this case, the possibility of tumor as the underlying cause of the blood must be considered, but there can be no doubt as to the blood having caused the immediate symptoms, and the interval of one year without symptoms makes the diagnosis of tumor unlikely. A similar case recently came under observation.

CASE 27.—Bloody cerebrospinal fluid with increased intracranial pressure and other signs suggesting tumor of the brain. Gradual improvement of symptoms as lumbar punctures were made.

C. C., a married man, aged 46, while at work was suddenly seized with severe pains in the head and was immediately taken to the hospital in an unconscious condition. There was postcervical rigidity and a positive Kernig sign. When he was examined, twenty-four hours after the onset of the trouble, the pulse was slow and the disks indicated an increase in intracranial pressure. Lumbar puncture revealed a bloody cerebrospinal fluid. In this case, the early change in the disk and the slow pulse rate with slow clearing up of the symptoms after puncture made one suspicious of something more than a little blood mixed with the cerebrospinal fluid, perhaps a tumor or large hemorrhage with some leakage into the subarachnoid space. Three weeks after the onset of the symptoms, the fluid was almost entirely clear; the patient was still somewhat confused, but gradually improved, following much the same course as that noted in case 24. It is now three months since the onset, and the patient is gradually improving; all signs and symptoms have disappeared, except dizziness and some unsteadiness of gait.

SUMMARY

Short clinical histories of twenty-seven patients with bloody cerebrospinal fluid are presented. In most of the cases, the blood in the fluid resulted from trauma, and the effect of the blood is shown in the acute, subacute and chronic stages.

In two cases, the blood was due to congenital venous anomalies, and in one case to a tumor of the brain present at the time of birth.

Five patients ranging in age from 12 to 44 years had aneurysms of the anterior cerebral arteries.

In four of the patients who recovered, the exact underlying causes could not be determined, but arteriosclerosis was the most probable factor.

COMMENT

The material has been collected for the purpose of demonstrating the acute and chronic changes in the central nervous system following the introduction of blood in the cerebrospinal fluid.

Cases in which there were meningeal irritations due to a free mixture of the blood with the fluid have been selected, and the discussion does not include cases in which the patients had large blood clots.

The symptoms immediately following the escape of blood into the cerebrospinal fluid depend on the amount of blood and vary from slight headache to severe pain with convulsive seizures and loss of consciousness. The most important signs and symptoms in patients with a small quantity of blood usually appear after an interval of a few days and are due to the reaction of the meninges. This state is characterized by headache of a neuralgic type, delirium, mild elevation in temperature, slight increase in pulse rate, postcervical rigidity and a positive Kernig sign. These symptoms may gradually subside as the blood is absorbed. In adults, complete recovery may take place, but infants presenting the early symptoms, if allowed to go untreated, frequently develop rigidity of the muscles and epilepsy. If the early symptoms progress, the signs of cerebral edema with evidence of marked increase of intracranial pressure may appear and may result in death.

An analysis of the signs and symptoms due to bloody cerebrospinal fluid impresses one with the importance of recognizing the condition, because the diagnosis in these patients may be confused with that in almost any of the common lesions of the brain from meningitis to tumor of the brain. In some cases, the disturbance due to the blood in the cerebrospinal fluid must be cleared up before the primary lesion can be diagnosed.

Treatment depends on the stage of the disease and should be carried out with the view of removing the irritating blood and preventing or relieving the meningitis. Absorption of some blood always takes place, but this is associated with meningeal thickening which may cause a block in the channels through which the fluid is returned to the blood stream. Treatment, therefore, has to do with the drainage of fluid which may be accomplished through lumbar puncture or the more radical procedure of decompression or even a bone flap. Some of the cases for this paper have been selected for the purpose of showing types suitable for the various procedures.

This work has been carried on under the direction of Dr. Adolph Meyer. Dr. Robert B. Wright assisted in the study of the specimens and Miss Cecelia Bisson made the illustrations.

BILATERAL LOBAR ATELECTASIS

REPORT OF A CASE WITH AUTOPSY OBSERVATIONS *

R. P. BALL, M.D.

CLEVELAND

This is a report of a case in which bilateral lobar atelectasis was associated with acute pancreatitis (fat necrosis). The observations made at autopsy suggest a probable explanation for the collapse of the lower lobes of the lungs.

REPORT OF A CASE

A woman, aged 48, who had enjoyed good health until October, 1925, developed symptoms of hyperthyroidism. A thyroidectomy was performed on Nov. 28, 1925. The gland showed slight hyperplasia. Preceding the operation, the basal metabolic rate was plus 56 per cent. In March, 1926, the basal metabolic rate was minus 21 per cent, and the patient showed other signs of hypothyroidism including obesity. After this time, thyroid extract was administered regularly.

Four months before her final admission to the hospital, the patient had intermittent colicky pains in the upper right quadrant of the abdomen, which were diagnosed as "gallbladder attacks." Three days before admission (Dec. 4, 1927), the patient had a severe persistent pain in the upper right quadrant of the abdomen, which became localized in the region of the gallbladder and was accompanied by vomiting. The pain was referred to the back and was described by the patient as being "between the shoulder blades." On December 7, the patient had a transient cyanosis which lasted for fifteen minutes and was characterized by rapid respiration and a feeling of impending danger.

On admission to the hospital, on December 8, the patient had a temperature of 38 C.; the pulse rate was 130 and the respiratory rate was 25. Physical examination revealed tenderness in the region of the gallbladder and a questionable tumor-like mass which appeared to be an empyema of the gallbladder. The lower lobe of the right lung was thought to be consolidated, and over the lower lobe of the left lung were heard numerous moist râles and tubular breathing. A diagnosis was made of empyema of the gallbladder with possibly bronchial pneumonia. Because of the serious condition of the patient, an exploratory operation was postponed.

The average white blood cell count while the patient was in the hospital was 16,000 per cubic millimeter. The red blood cell count was 3,400,000. Eighty-three per cent of the white blood cells were polymorphonuclear neutrophils. The urine was acid in reaction; the specific gravity was 10.10, and all specimens showed two plus albumin. There was no glycosuria and the microscopic examinations showed the constant presence of a few pus cells. A liver function test showed 1.2 mg. serum bilirubin. The blood sugar averaged 120 mg. per hundred cubic centimeters. Plasma carbon dioxide was 39 and the blood urea, 57. A culture of the sputum did not reveal pneumococci. A roentgenogram was reported as unsatisfactory (fig. 1), but because the patient was thought to have pneumonia there was some objection to making another roentgenogram.

On December 21, the abdominal tenderness became more generalized, and the abdomen appeared to be more distended than before. An exploratory

*From the Department of Pathology, Cleveland Clinic.

laparotomy was therefore performed on the patient without removing her from her bed. The operation was done under local anesthesia with procaine hydrochloride together with nitrous oxid-oxygen analgesia. An upper right rectus abdominal incision was made, and the peritoneal cavity was then exposed. The liver was found to be pushed over to the right and numerous adhesions between the anterior abdominal wall and the region of the falciform ligament were found. Many small, dull white, oval areas were scattered throughout the peritoneal cavity; these were more numerous on the omentum, a condition which is typical of fat necrosis. The lesser peritoneal cavity was distended with a pale red, serous fluid. An opening was made in order to drain the fluid, and a drain was placed in the region of the pancreas. Eight hours later, the patient ceased to breathe.

Necropsy Report.—An autopsy performed one hour post mortem revealed the following: The peritoneal cavity contained blood-stained serum and a blood



Fig. 1.—Bilateral lobar atelectasis; consolidation of the lower lobes.

clot. The falciform ligament was 4 cm. to the right of the midsternal line; the greater omentum was uniformly distributed over the intestines with the lower border at the pelvis. Numerous oval, dull white, discrete areas averaging 10 mm. in diameter were scattered throughout the omentum and peritoneal cavity; the tissue surrounding these areas was not discolored. On account of edema and of infiltration of the tissue surrounding the foramen of Winslow which produced mechanical obstruction between the two peritoneal cavities, the lesser peritoneal cavity did not communicate with the greater cavity. The lesser cavity contained about 3,300 cc. of blood-stained serous fluid in which were floating bits of debris.

When the sternum with the attaching costal cartilages was removed, the mediastinum was found in the midline. Both pleural cavities were clean. The dome of the diaphragm on the right was at the level of fourth rib, and on the left, at the level of the fourth intercostal space.

The pericardial cavity was clean. The apex of the heart was 10 cm. to the left of the midsternal line and at the fifth rib.



Fig. 2.—Lungs in case of bilateral lobar atelectasis. Note the relatively small lower lobes and the sharp line of demarcation of the atelectatic areas.

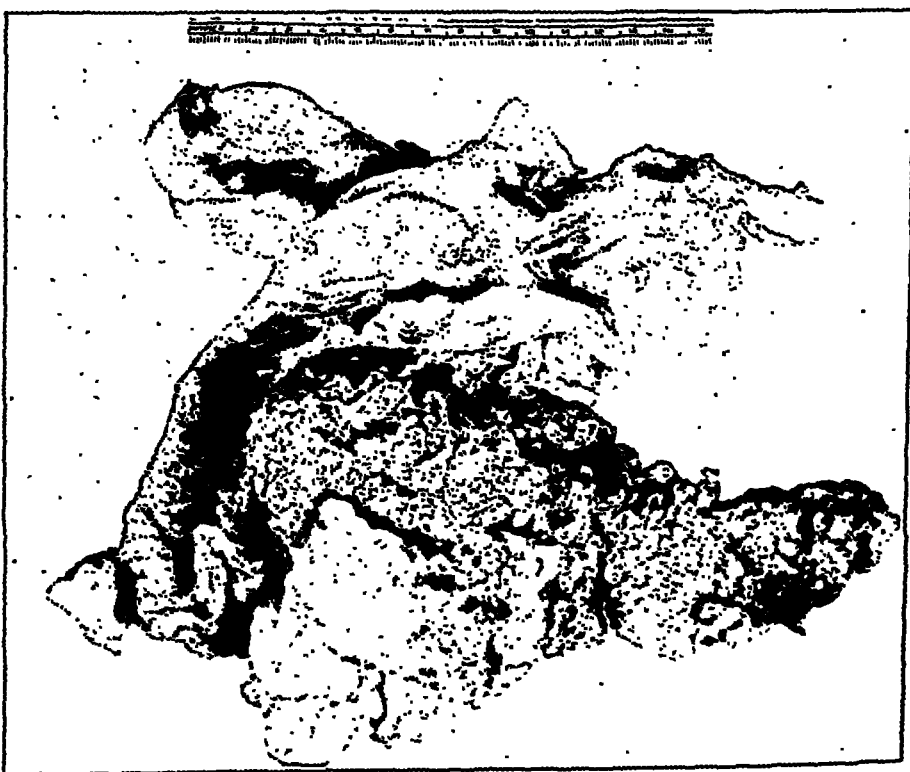


Fig. 3.—Pancreas with attached duodenum in case of acute pancreatitis—fat necrosis, associated with bilateral lobar atelectasis.

The left lung weighed 300 Gm., the right, 320 Gm. With the left lung in situ only a narrow margin of the lower lobe was visible. The upper lobe was of a pale bluish-gray cast with dull slate-colored mottling. The right lung in situ was similar to the left lung. The pulmonary artery was opened without disturbing the organs and was found to be normal. The trachea and the first division of the bronchi were opened and were found to be clean. The lower



Fig. 4.—Lobar atelectasis, showing obliteration of the alveolar spaces by apposition of the interalveolar walls; $\times 160$. Note that blood vessels are free from thrombi.

lobe of the left lung was limp, flabby and airless, and its pleural covering was clean and glistening except for a small area about 3 by 1 cm. which was covered with a loose fibrous adhesion. The cut surface of the lower lobe was homogeneous in appearance. A small amount of blood-stained material was obtained only on

continued scraping. The cut surface of the upper lobe was pale pinkish-gray and was moist. The right lung was similar to the left except that there was an atelectatic area at the base of the middle lobe which was identical in appearance with the lower lobe (fig. 2).

The pancreas was soft dark reddish-gray; it was friable and of about the same appearance throughout. On account of shaggy-lined crypts filled with friable, dark gray material, the surface was uneven (fig. 3).

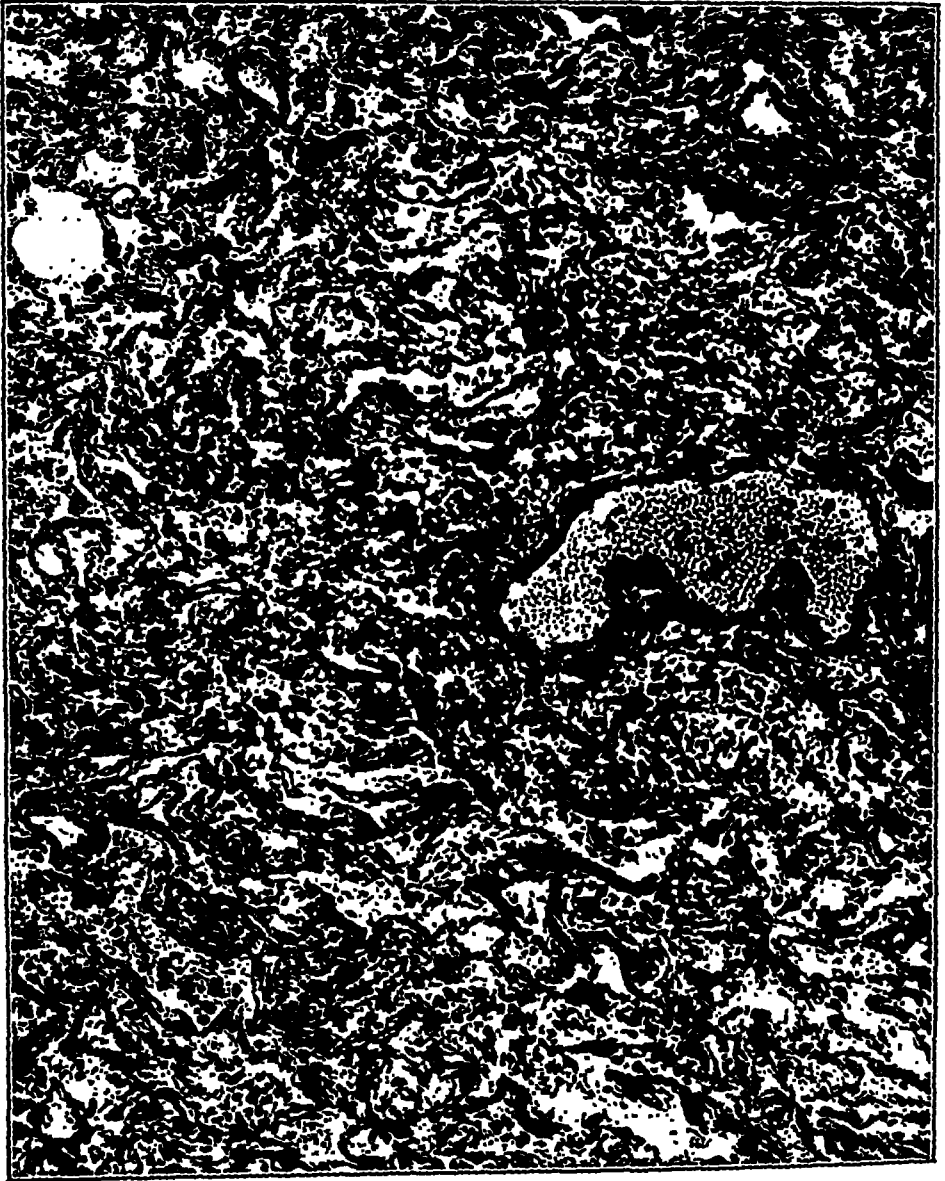


Fig. 5.—Lobar atelectasis, showing apposition of many of the interalveolar walls, and the presence of serum and red blood cells in the alveoli; $\times 160$. Note absence of thrombi in both arteries and veins.

The falciform ligament was 4 cm. to the right of the midsternal line. The lower border of the right lobe of the liver was 10 cm. below the costal margin in the right midclavicular line. The edges were slightly rounded and the surface of the organ was smooth. The cut surface showed normal lobular markings.

The serosa of the gallbladder was smooth and clean. The organ was slightly ballooned and was filled with dark tenacious bile containing numerous small soft yellowish faceted stones averaging 3 mm. in diameter. On squeezing the gallbladder, bile flowed from the ampulla of Vater.

Microscopic Observations.—Sections through the atelectatic area showed the interalveolar wall to be in apposition. Some of the alveoli of the lungs contained mononuclear leukocytes, serum and red blood cells. The bronchi contained mononuclear leukocytes. With the exception of the lining cells of the alveoli, which were more cuboidal, the alveoli were normal in appearance (figs. 3 to 5).

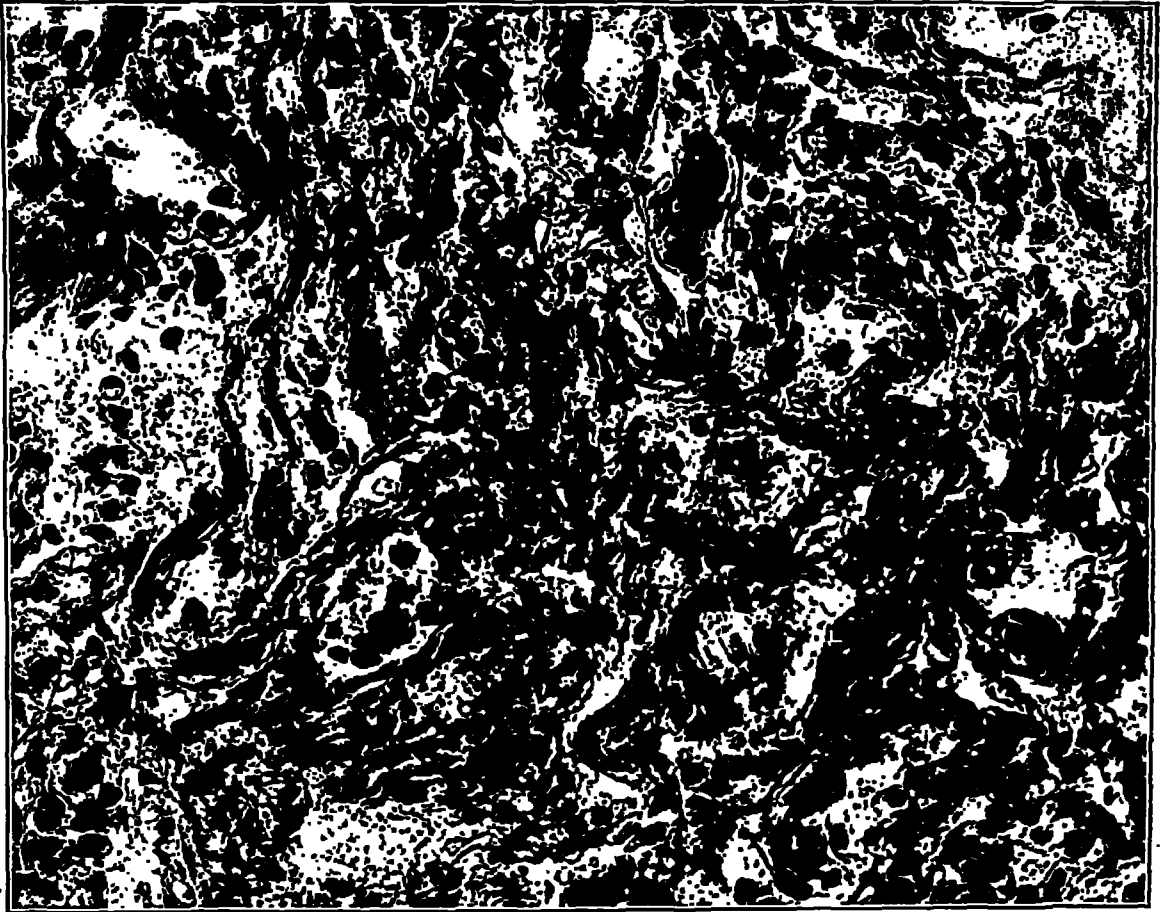


Fig. 6.—Lobar atelectasis, showing the lining cells of the alveoli have become cuboidal or rounded as the result of contraction of the alveoli; $\times 250$.

There were intact scattered islands of parenchyma in the pancreas which stained normally. The remaining tissue when stained presented a neutrophilic indistinguishable mass without histologic markings (necrosis). No leukocytic reaction was apparent except for an occasional clump of polymorphonuclear leukocytes at the periphery of the necrotic area (figs. 6 to 8).

Anatomic Diagnosis (Gross and Microscopic): The following anatomic diagnosis was made: (1) Acute pancreatitis (fat necrosis); (2) lobar atelectasis, bilateral; (3) cholecystolithiasis; (4) hydroperitoneum (ascites); (5) obstruction of the foramen of Winslow, and (6) recent laparotomy wound.

COMMENT

The term atelectasis is used here to denote the condition of the lung in a collapsed state. Although the term atelectasis of the lung is usually used to designate the complete or incomplete failure of the lung of the new-born to expand, nevertheless, no other term describes collapse of the lung of unknown etiology as well, especially when the etiology of this condition appears to be a lack of expansion, as shown in the foregoing case.

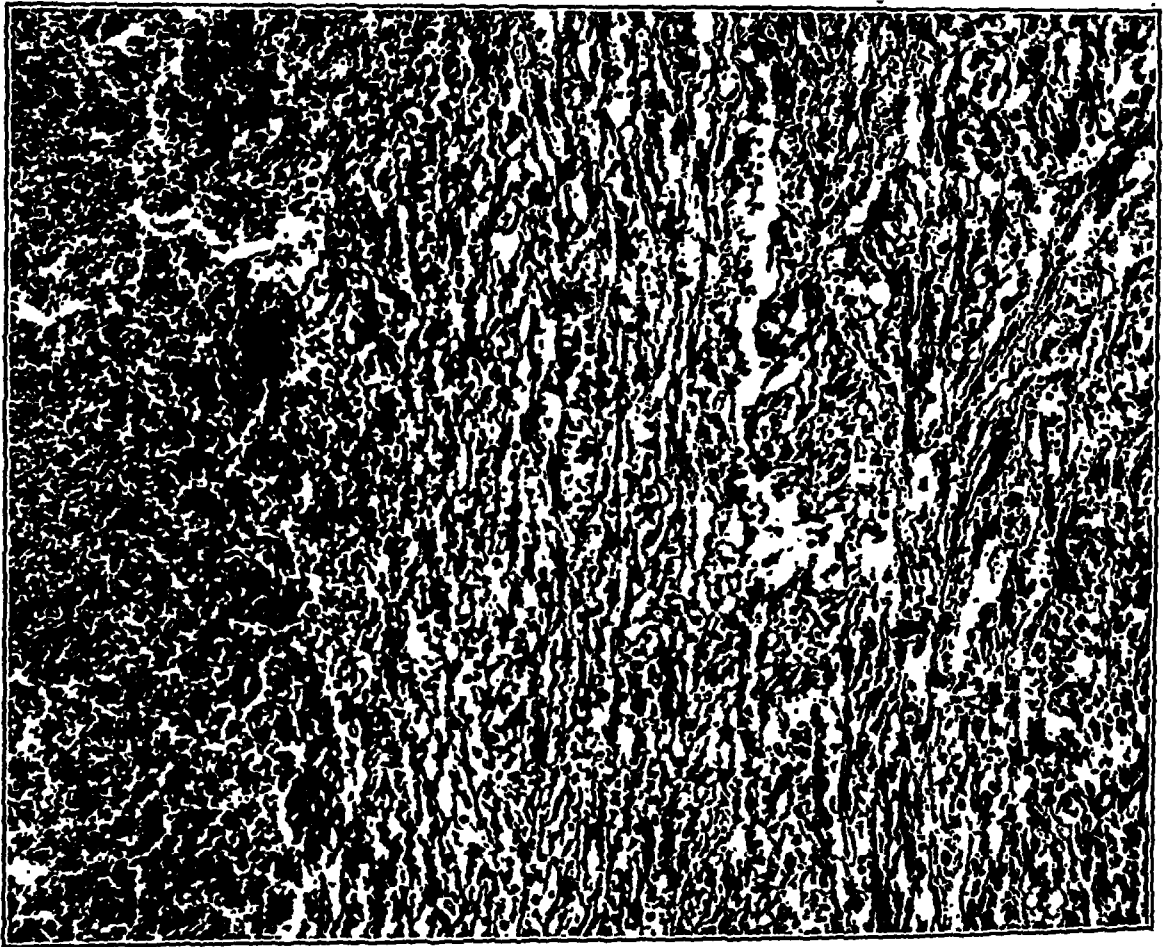


Fig. 7.—Acute pancreatitis—fat necrosis, showing absence of parenchyma and marked polymorphonuclear reaction; $\times 160$.

This lesion has never been experimentally reproduced except by ligating the bronchi. The use of plugs in a bronchi never produces atelectasis unless the bronchi are completely occluded. The severing of both phrenic nerves does not produce the lesion, nor is it found in many cases of paralysis of the diaphragm. An evident factor in the production of atelectasis which has not been considered, but which evidently is present, is fixation of the diaphragm. This factor we believe to have

been present in the case here reported. Keith¹ has called attention to the different factors concerned in the expansion of the upper and lower lobes of the lungs. The lower lobe is independent on the excursion of the diaphragm and lower intercostal muscles. The upper lobes are expanded by the action of the upper intercostals, the scaleni and the accessory muscles of respiration. It should be noted that paralysis of the diaphragm resulting from a lesion of the cord or from severing of the phrenic nerves does not prevent the ascent and descent of this

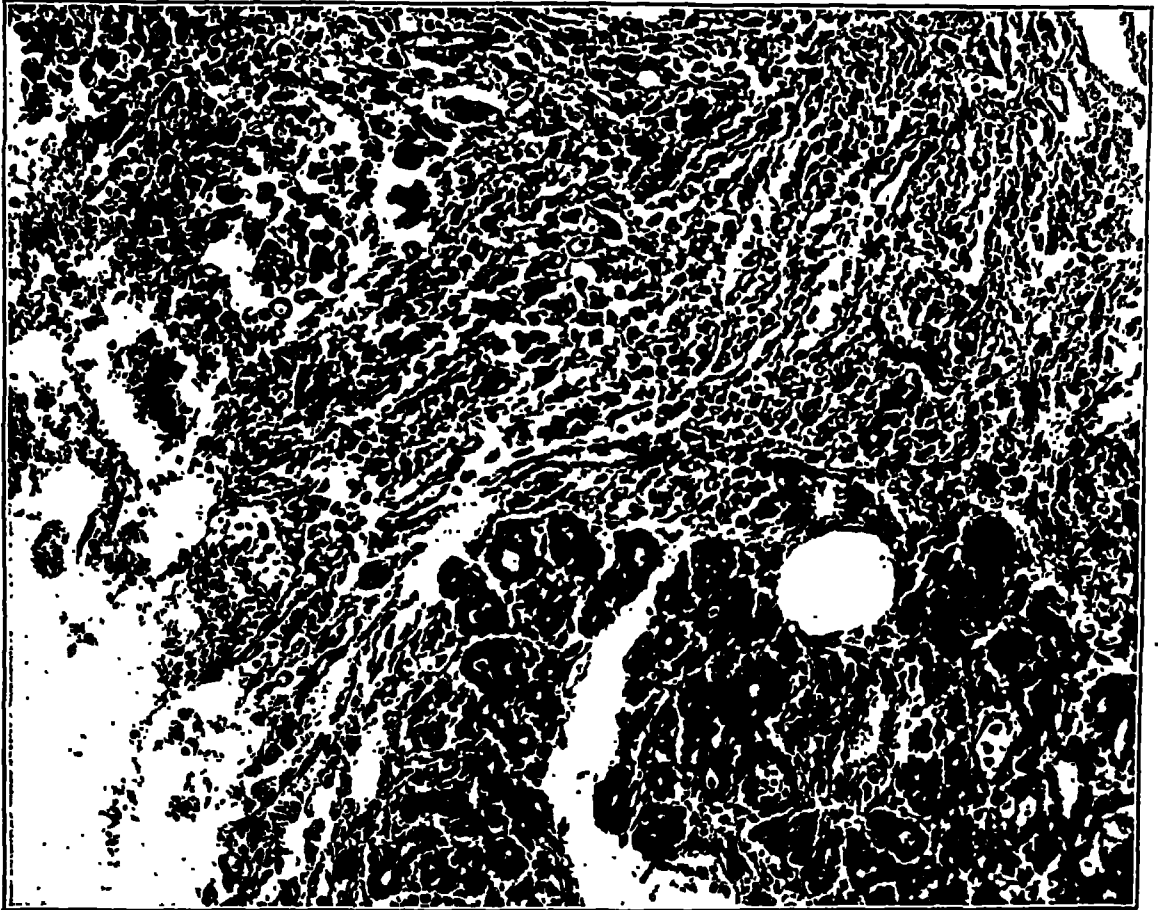


Fig. 8.—Acute pancreatitis—fat necrosis—, showing the presence of only a few parenchymatous cells; $\times 160$.

structure since it is then in a flaccid state and subject to intrapleural and intra-abdominal pressures. As in this case, fixation of the diaphragm evidently was present, the lesser peritoneal cavity was distended with fluid. Though the onset of the illness was evidently due to acute pancreatitis, three days later the patient had a transient cyanosis which is

1. Keith, cited by Soltan, A.: Massive Pulmonary Collapse, Brit. M. J. 1:544 (March 21) 1925.

typical of collapse of the lung. The roentgenogram taken five days after the acute onset of the illness shows what was probably a bilateral atelectasis of the lower lobes.

That the circulation continued through the atelectatic areas was well shown by the clean, glistening pleural surface and also by the well preserved structure of the interior of the lung. This of course would mean that a certain percentage of nonaerated blood returned to the left side of the heart. In the average patient, this deficient oxygenation of the blood would not be serious, but in cases of hyperthyroidism in which the oxygen consumption is greatly increased and also in cases of low cardiac reserve, this is a serious and sometimes a fatal complication.²

It is often stated in reports of cases of postoperative collapse of the lung that lobar pneumonia was a probable complication. In this case there was no pneumonic process and presumably the lungs in a patient of lowering resistance had been in a state of atelectasis for fourteen days. Impairment of the circulation in the atelectatic area was not sufficient to be evident.

SUMMARY

1. A case of bilateral lobar atelectasis in a woman, aged 48, is reported, the onset occurring three days after the onset of an acute pancreatitis (fat necrosis).

2. The observation that the lesser peritoneal cavity was distended with serum and the foramen of Winslow mechanically obstructed suggested the possibility that fixation of the diaphragm was the greatest factor in the production of a spontaneous collapse of the lower lobes of the lungs.

3. Collapse of either the upper or the lower lobe might be produced experimentally by removing all factors which are concerned in the production of the expansion of these lobes in the normal respiratory excursion.

2. Ball, R. P.: Lobar Atelectasis Following Thyroidectomy and Lobectomy; Report of Four Cases with Necropsy Findings, to be published later in *Arch. Path.*

SURGERY OF THE LUNG

CARE OF THE STUMP IN PNEUMECTOMY AND IN LOBECTOMY *

MINAS JOANNIDES, M.D.

Instructor in Surgery, University of Illinois College of Medicine

CHICAGO

Surgical treatment of the thorax is not a new field. Written records of thoracotomy in empyema and the recognition and drainage of pulmonary abscesses can be traced as far back as the time of Hippocrates in the fourth century B. C.¹ Hippocrates gave a detailed description of the course of pneumonia with the development of empyema and the steps of thoracotomy for the drainage of empyema. He recognized the development of pulmonary suppuration and regarded aspiration as the cause of it. After the time of Hippocrates, the subject was neglected until the beginning of the sixteenth century A. D., when Schenk, in 1584,² drew attention to this field. From that time on there were occasional reports of thoracotomies, and a great impetus was noticed with the introduction of methods of inducing artificial respiration by the Sauerbruch, the Brauer or the Meltzer technic. From this time on, thoracic surgery began its inception as a distinct specialty. In his brief but inclusive article, Willy Meyer³ classified various operations on the lung that had been devised up to that time under four headings:

1. A single mass ligature around the bronchus and its vessels; amputation; cauterization of the mucosa of the stumps with pure phenol or the Paquelin cautery.
2. A single elastic mass ligature around the hilum and the removal of the lung at a second procedure ten days later (Lenhartz).
3. Ligature and division of the main bronchus with the remnant of the lung tissue stitched over the stump (Garré).
4. Isolation and temporary clamping of the bronchus; curetting of the bronchus; tight silk ligature; a second loose catgut ligature placed more centrally around the bronchus (Friedrich).

Meyer described a method for pneumectomy that he had found successful. The steps of his procedure are as follows: (1) isolation of

* From the Department of Surgery, University of Illinois College of Medicine and Rush Medical College, University of Chicago.

1. Hippocrates: E. Littré Edition, 1851. *Περὶ τοῦτων τὸ δεύτερον*, vol. 7, chapter 44, p. 62, and vol. 7, chapter 57, p. 88; *Περὶ τῶν ἐντὸς παθῶν*, vol. 7, chapter 3, p. 174.

2. Schenk, quoted by Murphy, J. B.: *Surgery of the Lung*, J. A. M. A. **31**: 151 (July 23) 1898.

3. Meyer, Willy: *Pneumectomy with the Aid of Differential Air Pressure*. An Experimental Study, J. A. M. A. **53**:1978 (Dec. 11) 1909.

the bronchus, (2) clamping and crushing of the bronchus, (3) ligation and amputation and (4) burying of the stump and the use of top sutures. By using this technic, Meyer encountered only four deaths in twenty-one dogs on which total excisions of the lung were performed.

Other modes of handling the stump were developed from time to time. Thus, Halsted ⁴ performed twenty-one consecutive operations, and in only one was there primary infection of the pleura. He first isolated the bronchus; after bisecting it and removing the mucosa, he sutured the flattened edges together and held them with a series of sutures around the edges together with interrupted through and through sutures which encircled the cartilages.

Quinby and Morse ⁵ obviated the difficulty of pushing a large crushed portion of the main bronchus by treating each of the primary bronchi separately with the use of the technic employed by Willy Meyer.

Giertz ⁶ used a transplant of fascia lata to cover the crushed bronchial stump which was first sutured with silk mattress sutures.

Lilienthal ⁷ devised an ingenious technic for lobectomy. He applied a chain of pedicle suture ligatures and then excised the lung, leaving a generous stump. The ligatures were left long and were included in a rubber dam pocket, which prevented any of the remaining intrathoracic viscera from coming in actual contact with the stump. The rubber dam and the ligatures slough out and leave a healthy stump when they are removed.

It will be noticed that in practically all of the procedures mentioned little if any attention is paid to the vascular supply of the lung or the control of hemorrhage. I agree with Friedrich ⁸ that in surgical treatment of the lung hemostasis is the least troublesome factor, and that the success or failure of the operation depends on making a completely air tight stump. A few other factors must always be taken into consideration in operations on the lung. First, the lung expands and contracts with each respiratory movement so that the contiguous lobes interfere and make it necessary that they be packed away with wet gauze so that injury will not be produced. At times even a slight puncture with the needle or the tip of the knife causes an unnecessary amount of trouble-

4. Halsted, W. S.: *Clinical and Experimental Contribution to the Surgery of the Thorax*, Tr. Am. Surg. A. 27:119, 1909.

5. Quinby, W. C., and Morse, G. W.: *Experimental Pneumectomy: The Application of Data so Obtained to the Surgery of the Human Thorax*. Boston M. & S. J. 165:121, 1911.

6. Giertz, K. H.: *Ueber extirpation von Lungen und Lungenlappen mit Versorgung des Bronchial stumpfes durch frei transplantierte Fascia lata*, Zentralbl. f. Chir. 41:1433, 1914.

7. Lilienthal, H.: *Thoracic Surgery*, Philadelphia, W. B. Saunders Company. 1926, vol. 2, pp. 147-169.

8. Friedrich, P. L.: *Thoracic Surgery*, J. A. M. A. 53:1970 (Dec. 11) 1909.

some leakage of air and blood and makes it necessary to suture the lung by using either the Sauerbruch, Garré or a purse-string suture. Such an accident prolongs the operation and produces a greater tendency for shock and infection. Another important factor that aids in the success or failure of an operation on the lung is the length of time required. The quicker the operation is terminated, the better chance the subject has for recovery. By a mere thoracotomy the pressure relations of the intrathoracic and intra-abdominal organs are suddenly disturbed. In spite of the fact that intermittent positive pressure artificial respiration is maintained, and thus a stretching of the vessels of the lung provided for, as yet provision has not been made for the sudden increase of pressure exerted on the heart. Thus, the sudden and profound changes that occur in the circulation must be taken into account. I have often watched the heart become suddenly slow in rate and irregular in rhythm for no apparent reason, and only an injection of epinephrine or hydrochloride ephedrine would relieve this condition. In this case, if the heart is not stimulated promptly by means of an intracardiac injection of the drug, the animal either dies on the table or soon after the operation is performed. Another important factor that must always be considered is the sudden change in the temperature of the intrathoracic organs as a result of the thoracotomy. This sudden chilling undoubtedly has a definite injurious effect and must be prevented as much as possible. An important factor, indeed, is the manipulation and exposure of the virgin pleural cavity. The pleural surfaces are secretory and, like the peritoneal surfaces, any chemical, bacterial or mechanical irritation will produce an inflammatory change of a varying degree with subsequent exudation of serous fluid which has a tendency to change into a fibrinous and, later, a fibrous exudate, thus causing adhesions. The peritoneum has the same relation to the abdominal cavity as the pleura has to the thoracic cavity. It is inconceivable to think that a varying degree of pleuritis does not follow a thoracotomy. The most important consideration in surgical treatment of the lung is the upkeep of the process of oxidation in the body. I have found that dogs with an open pneumothorax do not live longer than ten minutes, at the most, after an intercostal opening of from 10 to 12 cm. Meltzer's insufflation anesthesia, which provides for a constant stream of air, is not satisfactory because it distends the lungs but does not make provision for contraction of the lungs. It is necessary that there be an intermittent blast of air so that an intermittent stretching and relaxing of the vessels of the lung may take place and thus the pulmonary circulation be kept up. In a series of experiments by means of which a sufficient amount of oxygen was supplied, a bilateral artery to vein transfusion being used, which was termed cross circulation, it was possible to double the length of life in the presence of an artificial pneumothorax. In these cases the lung stayed collapsed,

so that after the blood left the systemic circulation and entered the pulmonary circulation it encountered considerable resistance. As a result, a gradual engorgement in the lung of the recipient and a depletion of blood in the animal used as a donor were noticed. Thus, the donor died of an acute hemorrhage and the recipient of asphyxia and cardiac collapse. An intermittent artificial respiration obviates all this difficulty, because it not only supplies the lung with oxygenated air and provides for elimination of the carbon dioxide that is formed as a result of respiration, but it provides for the intermittent stretching and relaxing of the capillaries of the lungs that are so important in the welfare of the circulation of the blood.

Another factor of some importance is the disturbance to the vagus trunk of its branches as they enter the lung. In lobectomy, such as the Meyer type, one necessarily has to disturb the vagus. Under such conditions the heart, the circulation and the gastro-intestinal apparatus may be disturbed by the abnormal stimulation of the vagus. A factor recently was brought to my attention in some experimental lobectomies. In prolonged handling of the lung, an acute dilatation of the stomach, which proved fatal to the dog, was noticed. The difficulty was traced to a disturbance in the pillars of the diaphragm.⁹ This disturbance may result indirectly through the lungs or directly through injury to the phrenic nerve or disturbance of the diaphragm itself.

With these facts in mind it becomes evident that one must find a method which will be simple and can be completed rapidly. It should control both the aeration and the vascular supply of the lung. It should provide for the avoidance of any unnecessary chilling or drying of the intrathoracic organs. I feel that the technic that is proposed here will satisfy the majority of these factors.

PROCEDURE

After a preliminary shaving of the dog and cleansing of the skin with soap and water, the skin is sterilized with tincture of iodine. The animal is now covered with sterile sheeting, and only the field of operation is left exposed. An incision is now made in the skin parallel to the ribs, and the platysma and latissimus dorsi are exposed. These muscles are incised in the direction of their fibers and are spread open so that the least amount of injury is caused to the muscles. These muscles are later utilized to cover the intercostal incision tightly. The intercostal space now comes into view. At this point I make sure that the epinephrine or ephedrine solution is ready for instant use. I also have the anesthetist get the apparatus for administering artificial respiration ready. The artificial respiration is now started, and a small nick is made down into the chest. As soon as the pleura is pierced, one can hear a wheezing. The incision is now enlarged by means of the finger or a blunt instrument. At this point artificial

9. Hedblom, C. A., and Joannides, M.: The Relation of the Hiatus Esophageus to the Stomach. An Important Function of the Pillars of the Diaphragm, to be published.

respiration is stopped, so that the lung collapses, and in this way it is not torn when the intercostal incision is enlarged. This incision is usually made with the scissors. As soon as it is felt that a sufficiently large opening has been made in the chest, the artificial respiration is resumed and just enough pressure is exerted so that the lung expands and fills up the whole cavity of the chest.

The ribs are now spread apart with a self-retaining retractor, and the lung is pulled out by means of tissue forceps without teeth. At this point the artificial respiration is stopped again so as to allow the lung to collapse. Then a Kocher or Moynihan intestinal clamp with rubber tips is applied to the hilum (fig. 1). Just enough pressure is exerted with the clamp to stop the hemorrhage and control leakage of air when the lung is cut. Only a slight pressure is required for this clamping because the pressure in the lesser circulation is low, and the positive pressure in the artificial respiration apparatus is also low. Care must also be taken not to crush the tissues so that they will not slough. Artificial respiration is now started again and continued until the chest is closed.

Gauze moistened in hot saline solution is now used to protect the unexposed tissues and at the same time to catch any blood that will run out when the lung is cut. An attempt should be made to take out a wedge, and enough lung tissue must be left to cover over the stump (fig. 1). The lung should be cut at least 1 cm. distal to the compressing clamp. The bronchi are now isolated and ligated. The large vessels are also ligated. The suture is now started at the middle of the incision. This first suture is tied, but the end is left long so that it can be used later. A bite is now taken first on one and then on the other side of the first suture in such a way that the two sides of the wedge are brought in apposition. When the raw surfaces have all been covered with pleura, the compressing clamp is released and at the same time the suture is gently tightened. This maneuver accomplishes a double purpose. It allows the cut portions of the lung to become approximated more tightly, and at the same time it gives one an opportunity to look for leakage of air or blood. If the stump is airtight and watertight, the compressing clamp is removed and the chest is closed. If, on the other hand, the stump is leaky, the compressing clamp is retightened and additional interrupted sutures are used to cover the defect. The clamp is now removed, and the stump is left to drop back in the chest. Any blood that has found its way in the chest is now removed, and the chest is closed. In some experiments, the phrenic nerve is cut just before the chest is closed in order to produce a paralysis of the diaphragm and thus reduce that chance for suction through the stump. If the phrenic nerve is cut, care must be taken to ligate the pericardiophrenic artery, which is intimately attached to the nerve. In one case death was caused by hemorrhage from this vessel. Three fine wires are now used to aid in the approximation of the ribs. As they are inserted in the intercostal spaces with a number 1 or number 2 cutting needle, the underlying tissues are protected by means of a spatula which is placed on the parietal surface of the wall of the chest. In addition to the wire sutures, three interrupted heavy silk sutures are placed with the wires. The wires are pulled together, and thus the ribs are approximated. The silk sutures are tied and as soon as it is noticed that wheezing does not occur with each respiration, the artificial respiration is stopped. The overlapping muscles are now approximated and the wound is closed without drainage.

Care must be taken not to handle the heart or the pericardium any more than is necessary, because even the slightest handling has caused definite cardiac irregularity in the rhythm. The heart must be watched at all times and as soon as any slowing in the rate associated with cyanotic blood is noticed more air must

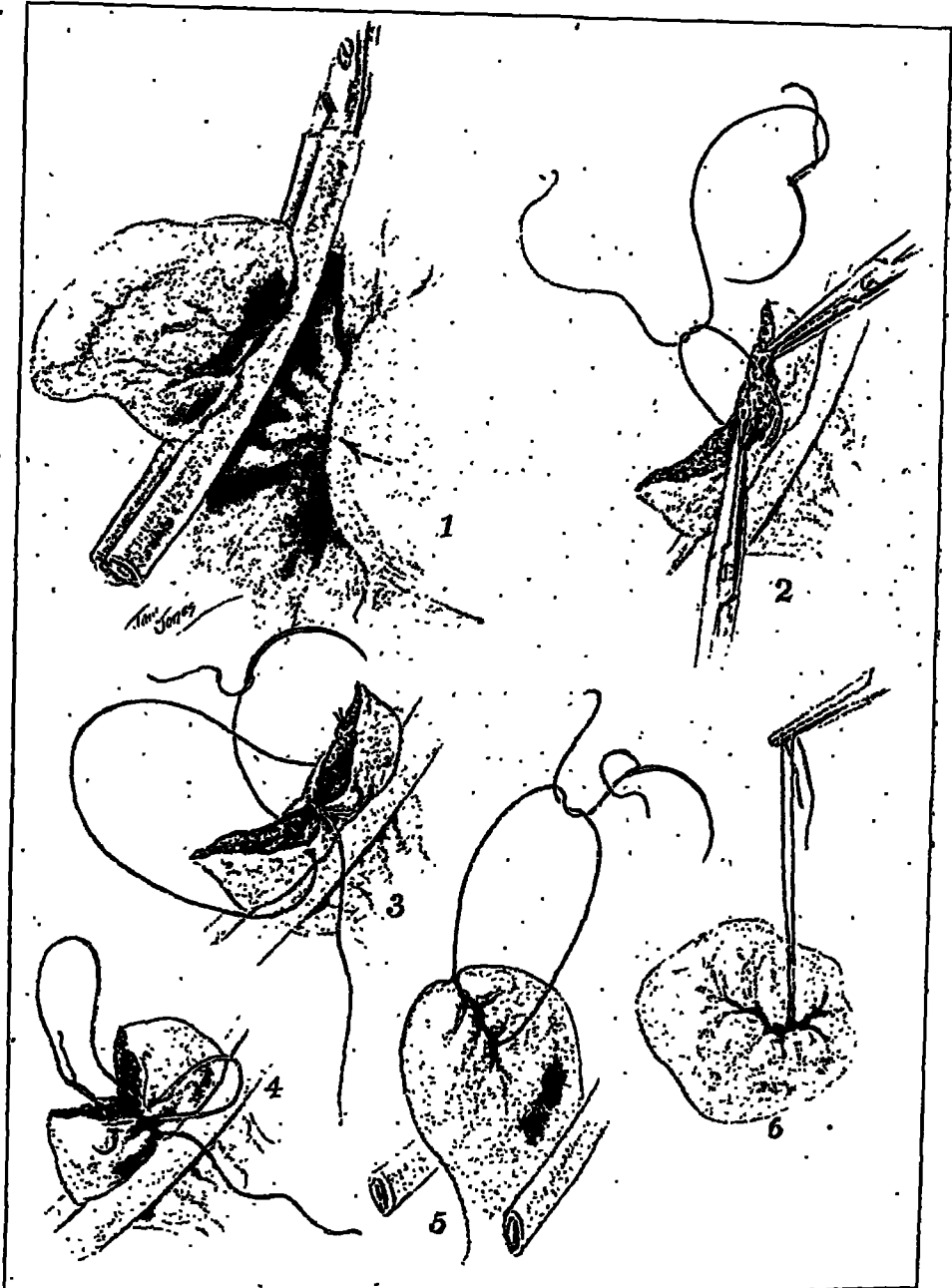


Fig. 1.—The important steps in the care of the stump. In 1, the arrow indicates the constricting clamp applied to the root of the lung; 5 shows the constricting clamp released and the suture tightened and 6, the appearance of the stump after the final knot is tied.

useful in the treatment of toxic abdominal distention, so-called. Bartlett,²⁸ too, found the employment of a dosage of 1/25 grain (0.002 Gm.) to give beneficial effects.

Cross²⁹ also advocated the use of the drug clinically combined with alternating doses of solution of pituitary, and at the same time gave experimental proof of his conviction by suspending a portion of the human appendix in Locke's solution and adding eserine and solution of pituitary, alternately. A stimulative effect is observed that is greatly

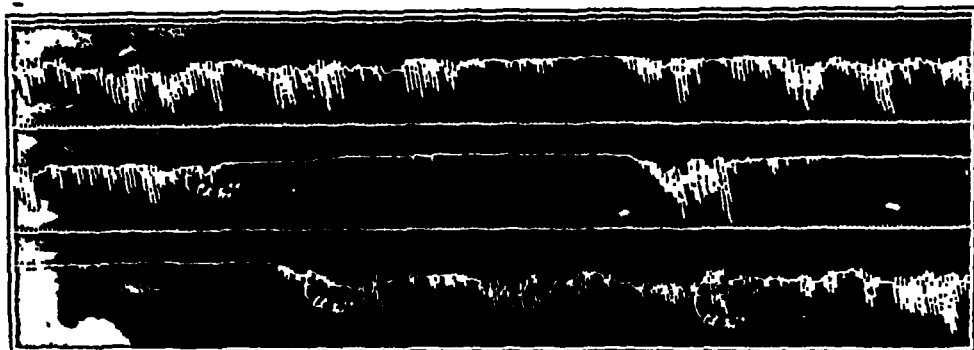


Fig. 5 (O. P. 34).—Record for dog obstructed for 165 hours. The top tracing shows a normal record; the second shows the effect of 0.025 cc. of pituitary fluid given intravenously. The third reveals that a repetition of the same dose does not produce any effect.



Fig. 6 (O. P. 36).—Record for dog obstructed for forty-eight hours. The normal tracing was for twenty minutes with maximum pressure of 32 cm. of water. The second tracing shows the effect of 0.5 cc. of oxytocin given intravenously, and the third of 0.4 cc. given intravenously twenty minutes later. The pressure was 5 cm. of water.

augmented by the addition of the second drug, no matter whether the eserine or the solution of pituitary is first employed.

28. Bartlett: *After-Treatment of Surgical Patients*, St. Louis, C. V. Mosby Company, 1918, p. 128.

29. Cross: *Brit. M. J.* 1:9, 1924.

THE DEVELOPMENT OF BONE

- (A) THE PROCESS OF DEVELOPMENT IN BONES OF DIFFERENT TYPES;
(B) NORMAL PHYSIOLOGIC CALCIFICATION OF THE MATRIX
IN CARTILAGE AND IN BONE; (C) THE PROBLEM OF
THE MANNER OF DEPOSITION OF THE
CALCIUM SALTS

JAMES CRAWFORD WATT, M.D.

Associate Professor of Anatomy, University of Toronto
TORONTO

In the studies here recounted, three different aspects of the problems involved in the development of bone are discussed, as indicated in the title. All three studies are closely interwoven and cannot be considered separately without much needless repetition and reduplication. Consideration is given each aspect in its proper relation to various portions of the work to be described, and they must be considered collectively for a proper elucidation of the problems discussed and for an interpretation of the results of the work which has been accomplished.

The process of the transport of calcium salts in the body and their deposition in bone have already been discussed in previous papers. But a much more thorough, detailed and minute study has now been made of the process of calcification of the cartilaginous and bony matrix of the skeleton, and the results obtained are embodied in this paper. It is to be remembered always that this calcification is a normal, physiologic process, and the conclusions arrived at by its study are far different from those derived from an examination of the pathologic process of calcification in various other tissues. A discussion of my views on the pathologic process is contained in a paper recently published,¹ showing that calcification in this case is a physical process of precipitation into dead or injured tissues and is not a function of the tissue cells. On the contrary, in the development and growth of the skeleton it will be shown that calcification is a function of the living cells and is dependent on their activity for its occurrence.

MATERIAL

Bones in process of ossification were examined in their earliest stages by means of serial sections of young human embryos aged from 6 to 12 weeks. Formation of bone both in cartilage and in membrane was conveniently followed here, especially in the skull, without decalcifying.

Later stages were obtained by sectioning the humerus, radius, ulna, ribs and parietal bones from human fetuses of various ages from 4 to 9 months, and also

1. Watt, J. C.: Deposition of Calcium Salts in Areas of Calcification, Arch. Surg. 15:89 (July) 1927.

The dose that we have administered was either 1/50 or 1/150 grain (0.001 or 0.0004), given for the most part intramuscularly. The only intravenous injections were made when 1/150 grain was used, all of which resulted in a definite increase in the intestinal motility except on one occasion when only a slight stimulative effect was noted. Following the intramuscular injections of 1/50 grain, there was a period of fifteen minutes, corresponding to the period of absorption, during which the intestines pursued their usual activity. A gradual rise in the intra-intestinal pressure then occurred, with subsequent abrupt increments, followed by a drop that was less in extent than the preceding rise until the pressure reached well above 100 cm. of water. This is much greater than is experienced in animals that have not been subjected to such stimulation, when it is rare to encounter a pressure greater than 50 cm. This period of increased intestinal motility continues for at least thirty minutes and may last an hour or even longer, though the usual duration is forty-five minutes. As

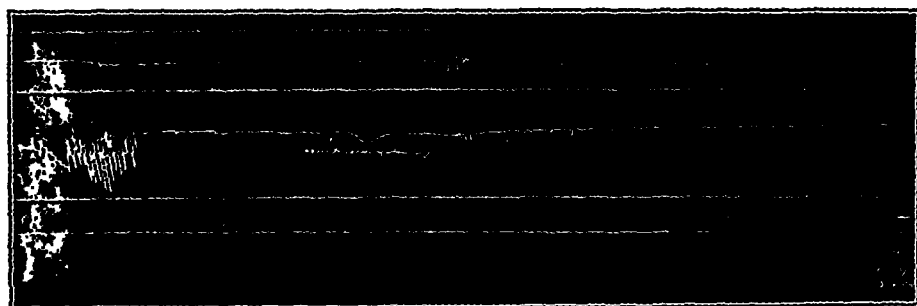


Fig. 7 (O. P. 36).—Record for dog obstructed for fifty-two hours. The normal motor activity is shown at the beginning of the second tracing when the pressure maximum is 30 cm. of water. After 0.25 cc. of vasopressin was injected intravenously there was little activity and none during the third tracing. The pressure was from 4 to 6 cm.

TABLE 2.—*Effect of Eserine Sulphate on Intra-Intestinal Pressure During Obstruction of the Small Bowel*

| Dog | | Drug | Quantity, Grain | Method of Injection | Maximal Intra-Intestinal Pressure, Cm. Water | | Duration of Effect, Minutes |
|------------------|-----------------------|---------|--------------------|------------------------|--|-------|--------------------------------------|
| Serial Number | Hours Ob- structed | | | | Before | After | |
| OP 27 | 25 | Eserine | 1/50 | Intramuscularly | 2-4 | 100+ | 25+ |
| OP 27 | 31 | Eserine | 1/150 | Intravenously | 6 | 6-8 | 10 |
| OP 27 | 31½ | Eserine | 1/150 | Intravenously | 6-8 | 28 | 10 |
| OP 32 | 32 | Eserine | 1/150 | Intramuscularly | 6-8 | 42 | 15 |
| OP 27 | 50 | Eserine | 1/150 | Intravenously | 10-32 | 100 | 30 |
| OP 27 | 53 | Eserine | 1/50 | Intramuscularly | 8-10 | 93 | 40 |
| OP 27 | 73 | Eserine | 1/50 | Intramuscularly | 2-5 | 105 | 30 |
| OP 27 | 100 | Eserine | 1/50 | Intramuscularly | 10 | 80 | 40 |
| OP 27 | 138 | Eserine | 1/50 | Intramuscularly | 6-8 | 114 | 15+ |
| OP 28 | 25 | Eserine | 1/50 | Intramuscularly | 2-4 | 26 | 30 |
| OP 29 | 22 | Eserine | 1/50 | Intramuscularly | 6-8 | 22 | 20+ |
| OP 33 | 92 | Eserine | 1/50 | Intramuscularly | 44 | 60 | 50 |
| OP 31 | 77 | Eserine | 1/50 | Intramuscularly | 6-8 | 68 | 70 |

similar specimens from young rats, some of which were new-born. For short and irregular shaped bones the tarsal bones of human fetuses aged from 6 to 9 months and those of children up to one month after birth were used, the navicular, cuboid, talus and calcaneus of one individual forming a set of four different stages valuable for comparisons. In these bones, ossification occurs as follows: the calcaneus in the sixth month, the talus in the seventh and the cuboid in the ninth month of intra-uterine life, and the navicular long after birth, usually in the fourth year.

TECHNIC

For the earliest stages small embryos were cut as a whole, while only the skulls of larger ones were used. For later stages, long bones were cut across the shaft so as to obtain about 5 mm. of bony shaft along with the cartilaginous epiphyses. Such a specimen was then split longitudinally and contained unaltered cartilage, calcified cartilage and newly formed bone in serial order in the section. Parietal bones were sectioned both transversely and tangentially. Tarsal bones were sectioned in their long axis, some of them serially.

All specimens were preserved in formaldehyde saline solutions and were sectioned without decalcifying so as to preserve calcium deposits intact. Duplicate specimens of some were decalcified to provide for ordinary histologic examination. All parts of the specimens remained intact on sectioning except for the hard, fully ossified shafts of long bones or the large ossified centers of some tarsal bones, which either broke somewhat or else slightly separated from the rest of the specimens at the line of junction with the calcified cartilage. Sections were cut 10 microns thick when possible, but when cutting was difficult they were made slightly thicker.

It is to be noted that there is a distinct difference in consistency between calcified cartilage and bone. Bone can be cut only with great difficulty, and only small areas of it can be gone through by the microtome knife without spoiling the sections and without danger of serious injury to the knife. Calcified cartilage is much softer and can be sectioned fairly easily.

In every case some sections were left unstained for both light and dark-field examinations, while other sections of each specimen were stained with hematoxylin and eosin and some with Mallory's triple stain.

I. PHYSIOLOGIC CALCIFICATION OF CARTILAGE PRECEDING OSSIFICATION

Preliminary to the occurrence of ossification in the skeleton there is a primary, rapid and transitory process of calcification in the cartilage about to be changed into bone. This process will be described in several different locations, and as it is best seen in the long bones formed in cartilage the conditions here will be first described.

Calcification of Cartilage in Shaft of Long Bones.—At the time when the budding blood vessels carrying osteoblasts with them invade the cartilaginous shaft of the future long bone in order to initiate ossification, the cartilage is seen to exhibit several well marked zones displaying different characteristics. These areas will be enumerated in order, passing toward the center of ossification.

At the extremities of the future bone (fig. 1, plate I), the cartilage cells are small and deeply stained and lie in a dense matrix which also

might be reasonably expected, the smaller doses have a correspondingly shorter period of effectivity. The figures followed by a plus sign in table 2 under the heading "Duration of Effect" do not represent the true period of action in all probability. At these times either another counteracting drug was injected, or the tracings and observations were discontinued.



Fig. 8.—Fresh longitudinal sections of dog's intestine cut from a normal animal under amytal anesthesia. The uppermost tracing shows the effect of 0.05, 0.2 and 5 cc. of pituitary fluid; the middle tracing shows the effect of 0.1 and 2 cc. and the lowest tracing shows the effect of 0.2 and 1 cc.



Fig. 9.—Effect of 0.5, 1 and 2 cc. of pituitary fluid in longitudinally suspended portions of a dog's intestine that had been obstructed 100 hours.

Corresponding to the solutions of pituitary there are also definite constitutional or general systemic responses. The chief of these is a twitching of peripheral skeletal muscle. This effect, in some instances, is violent. The other obvious physiologic responses were contraction of the pupil, salivation, slowing of the pulse and occasional vomiting. On two occasions pituitary fluid was given before the injection of eserine. In these instances, the muscle twitchings were much less and the intestinal motility not so violent and more normal in type.

stains well. Next to this lie zones in which the cells become progressively larger and more irregular in disposition and in which the staining of the matrix becomes paler.

Succeeding this, there is an area of transition terminating in the zone in which the enlarged cartilage cells lie close together in large lacunae arranged in columns. Between the cells of a column lie thin trabeculae of cartilage, while between contiguous columns lie heavy trabeculae of matrix. The cells of this area stain irregularly, and many appear to be degenerating and dying as the line of newly forming bone is approached. The matrix of this zone is heavily calcified and stains deeply with hematoxylin.

The final area seen in the specimen is one containing the primary marrow spaces with large blood vascular-sinuses separated by trabeculae of calcified cartilage. On the latter, spicules of new bone are being deposited by the osteoblasts which were brought in with the blood vessels and now line the surface of the trabeculae.

On examining the calcium deposited in such a specimen as that described, one finds that in the bony spicules it is finely granular and requires fairly high magnification to reveal its nature. The cartilage trabeculae on which bone is being formed and the area of calcified cartilage immediately in advance of the line of ossification both exhibit a dense impregnation with calcium salts in the form of much coarser granules, which are all contained within the matrix. An interesting point in this connection is that around each lacuna there seems to be a thin layer of matrix which might be interpreted as the capsule for the cartilage cell, and this capsule does not contain visible calcium salts. The clear wall which is thus formed around each space is quite noticeable.

If stages previous to the occurrence of the center of ossification are examined, the processes which terminate in the calcification of the cartilage may be followed from their beginning. The earliest appearance of a change in the normal cartilage consists of two elements, first an increase in the size of the cartilage cells, and second, a matrix which becomes pale and no longer stains well.

Marking the next stage the cartilage cells arrange themselves in groups, and between contiguous groups the amount of matrix is fairly heavy and forms a substantial, branching, trabecular network. This matrix is darker again, staining fairly deeply, and indicates the areas which in later stages become most heavily calcified. These are destined to be the supporting trabecular network of calcified cartilage which is not eroded during the process of ossification but which remains as a sort of scaffolding on which newly forming bone is deposited in the ossifying area.

HYPERTONIC SODIUM CHLORIDE

Among the first investigators to emphasize the value of sodium chloride in intestinal obstruction were Hartwell and Hoguet.³⁰ These workers found that the giving of physiologic sodium chloride solution to dogs with duodenal obstruction increased their life from a few days to about three weeks. In 1920, MacCallum and others³¹ also noted that a large supply of chlorides prevented the symptoms of pyloric obstruction and restored the plasma chlorides to their proper level. Haden and Orr³² were the first to investigate in detail the changes in the blood chemistry, which they found were most marked in high intestinal obstruction. To dogs they gave 50 cc. of a 10 per cent solution of sodium chloride with good results, but had animals live twenty-one and twenty-eight days when they gave 500 cc. of a 0.85 per cent solution daily. In one instance, the animal died soon after

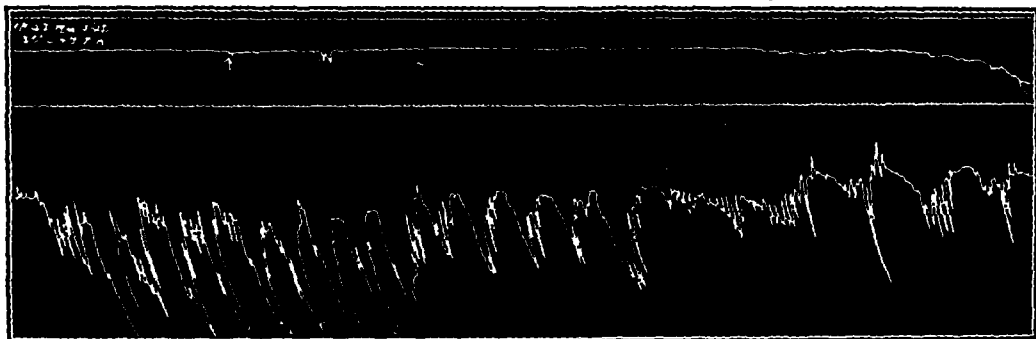


Fig. 10 (O. P. 27).—Record for dog obstructed for seventy-six hours. The arrow on the upper tracing shows the effect of $\frac{1}{60}$ grain (0.0013 Gm.) of eserine sulphate given intramuscularly. Note the intestinal activity after fifteen minutes and still present at the end of the tracing, thirty-five minutes. The intra-intestinal pressure reached a maximum of 106 cm. of water.

an injection of a 25 per cent solution. Hughson and Scarff³³ were able to show experimentally that hypertonic salt solution not only prevents absorption from the intestine but also stimulates peristalsis, while its use in two clinical cases of paralytic ileus proved a great success after pituitary had failed completely. Ross,³⁴ also, both experi-

30. Hartwell, J. A., and Hoguet, J. P.: *Experimental Intestinal Obstruction in Dogs with Especial Reference to the Cause of Death and the Treatment by Large Amounts of Normal Saline Solution*, J. A. M. A. 59:82 (July 13) 1912.

31. MacCallum, Linty, Vermilego, Lyett and Boas: *Bull. Johns Hopkins Hosp.* 31:1, 1920.

32. Haden and Orr: *Bull. Johns Hopkins Hosp.* 24:26, 1923; *J. Exper. Med.* 38:55, 1923; *Surg. Gynec. Obst.* 37:465, 1923.

33. Hughson and Scarff: *Bull. Johns Hopkins Hosp.* 35:197, 1924.

34. Ross: *Canad. M. A. J.* 16:241, 1926.

PLATE I

Fig. 1.—Longitudinal section of the phalanges of the finger of a seven months human fetus, showing developing bone in the shaft; $\times 8$.

Fig. 2.—Longitudinal section of the upper end of the humerus in a seven months human fetus. Note the numerous blood vessels in the cartilage forming the epiphysis, in which ossification does not commence until several months after birth; $\times 8$.

Fig. 3.—Longitudinal section of the elbow joint of a seven months human fetus. Blood vessels are numerous in the cartilaginous ends of the bones, which do not ossify until years after birth; $\times 8$.

All the illustrations are from photographs of specimens stained with hematoxylin and eosin except figure 10, in which the stain used was silver nitrate. The arrow, when used, points toward the center of the bone. In all the figures, *A.C.* indicates altered cartilage; *B.T.*, bone trabecula; *B.V.*, blood vessel; *C.C.*, cartilage cell; *C.C.T.*, calcified cartilage trabecula; *C.O.*, center of ossification; *G.D.*, granular deposit of calcium salts; *L.*, lacuna; *L.U.T.*, large, uncalcified trabecula; *L.W.*, lacunar wall free from granular deposit; *M.*, matrix; *P.*, periosteum; *P.M.C.*, primary marrow cavity; *S.T.*, stained trabecula and *U.C.*, unaltered cartilage.

mentally and clinically found hypertonic saline a great intestinal stimulant. Coleman,³⁵ in a review of his cases, found that the giving of 3 quarts of a 3 per cent solution reduced the mortality from 50 to 11.1 per cent.

In our studies we gave intravenously either 5 or 10 cc. of a 25 per cent solution. In all but one instance, we found a stimulative response. Generally, not only is there a rise in the intestinal tone, as is shown by an increase in the average rise of the intra-intestinal



Fig. 11 (O. P. 27).—Record for dog obstructed for 132 hours, showing the effect of $\frac{1}{60}$ grain (0.0013 Gm.) of eserine sulphate given intramuscularly. The intra-intestinal pressure had reached 114 cm. of water when 1 cc. of pituitary fluid was given intravenously. Note the marked cessation of movement and the fall in pressure.

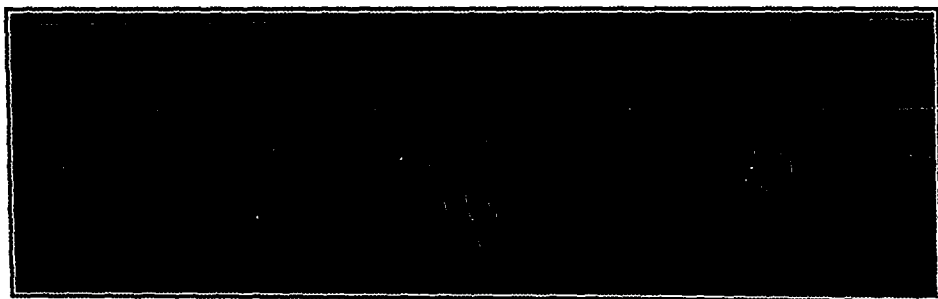


Fig. 12 (O. P. 34).—Record for dog obstructed for seventy-eight hours. The upper tracing shows a late effect (30 to 50 minutes) after 1 cc. of pituitary prepared by Park, Davis Company was injected. The lower tracing shows the effect of $\frac{1}{60}$ grain (0.0013 Gm.) of eserine intramuscularly in the same dog fifteen minutes later. Note that the muscular activity is not so great as usually occurs after administration of eserine.

pressure, but the maximum levels are well above the normal. The duration of activity is generally about from twenty to thirty minutes. The motor activity is not so violent as after the administration of

35. Coleman, E. P.: Use of Hypertonic Saline Solution in Acute Intestinal Obstruction, J. A. M. A. 88:1060 (April 2) 1927.

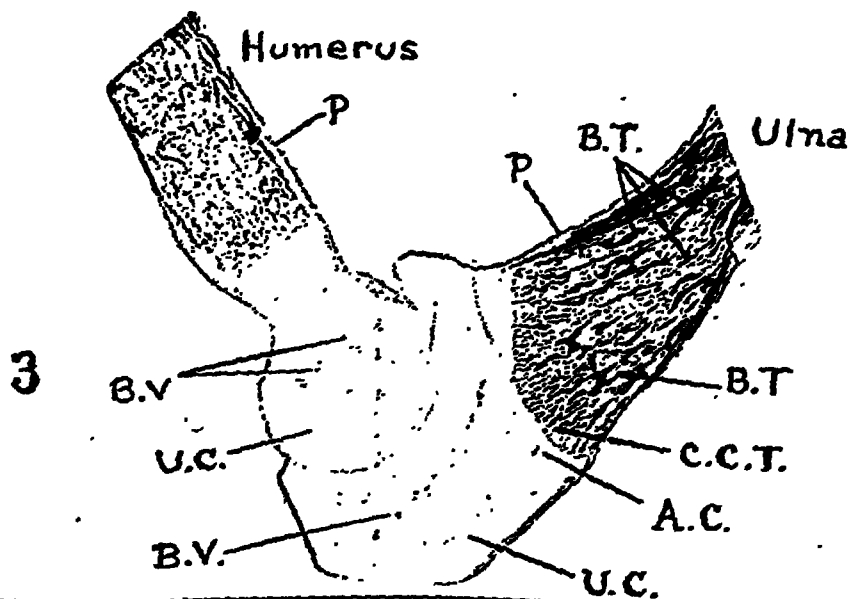
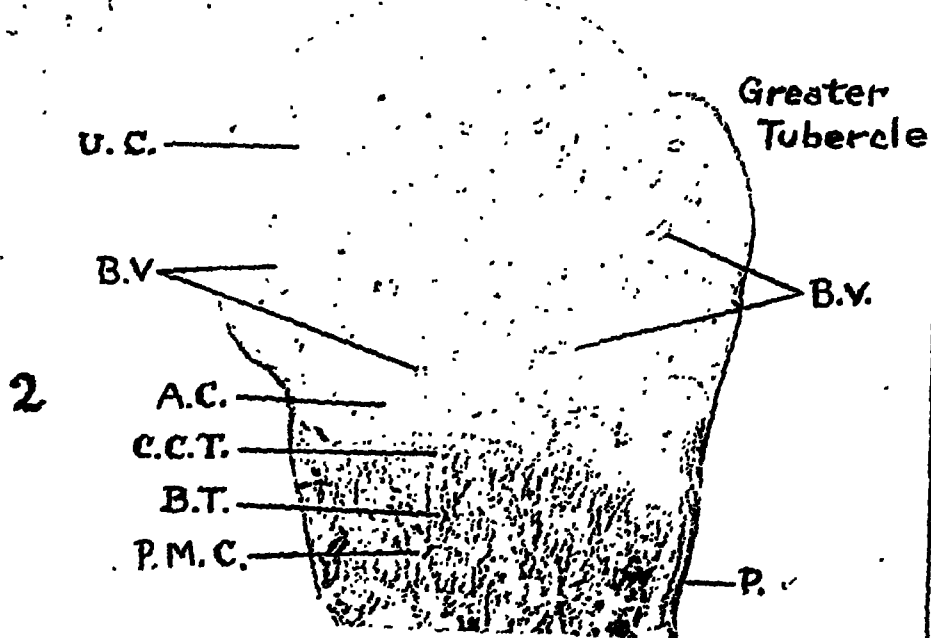
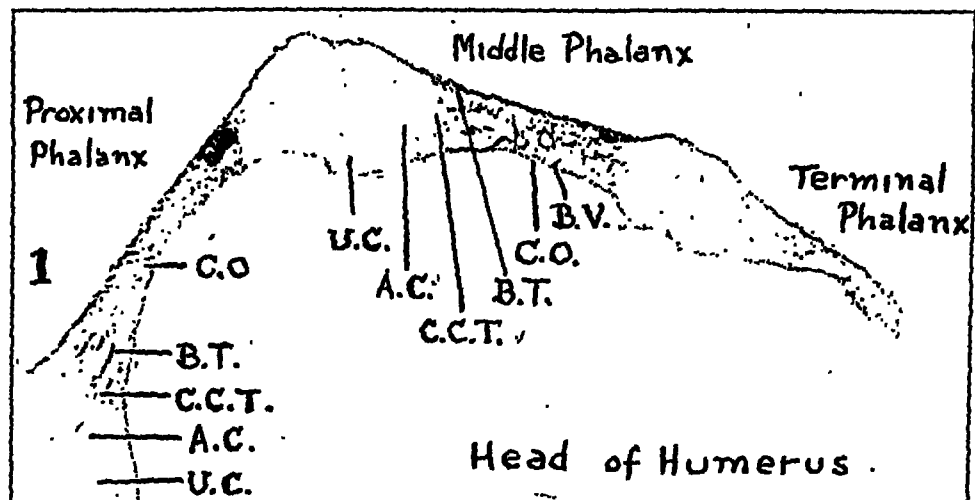


TABLE 3.—*Effect of Hypertonic Sodium Chloride on Intra-Intestinal Pressure During Obstruction of the Small Bowel*

| Serial Number | Dog Hours Obstructed | Sodium Chloride, per Cent | Quantity, Cc. | Method of Injection | Maximal Intra-Intestinal Pressure, Cm. Water | | Duration of Effect, Minutes |
|---------------|-------------------------|---------------------------|---------------|---------------------|--|-------|-----------------------------|
| | | | | | Before | After | |
| OP 27 | 48 | 25 | 5 | Intravenously | 14-16 | 28 | 10 |
| OP 27 | 49 | 25 | 5 | Intravenously | 6 | 18 | 20 |
| OP 27 | 136 | 25 | 10 | Intravenously | 2-4 | 10 | 30 |
| OP 28 | 7 | 25 | 10 | Intravenously | 2-4 | 2-4 | .. |
| OP 28 | 20 | 25 | 10 | Intravenously | 2-4 | 26 | 10 |
| OP 29 | 22 | 25 | 10 | Intravenously | 2-4 | 32 | 20 |
| OP 33 | 77 | 25 | 10 | Intravenously | 2-4 | 54 | 25 |
| OP 33 | 96 | 25 | 10 | Intravenously | 30 | 36 | 30 |
| OP 34 | 106 | 25 | 10 | Intravenously | 10 | 70 | 30 |
| OP 34 | 187 | 25 | 10 | Intravenously | 5-6 | 58 | 25+ |

eserine, and the type of graph has the appearance of an increase in the normal rather than the changed character to the tracing obtained from eserine. In other words, the same rhythmic activity is found

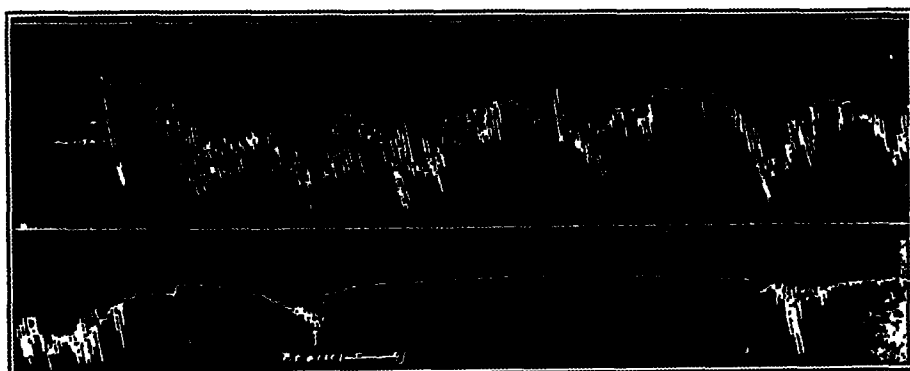


Fig. 13 (O. P. 34).—Record for dog obstructed for 120 hours, showing the stimulative action of 10 cc. of 25 per cent sodium chloride intravenously. The intra-intestinal pressure rose to 57 cm. of water. The lower tracing shows the result of giving 1 cc. pituitary fluid.

after hypertonic saline is given as is found normally, except that the maximum change in pressure is greater than normal.

Ergotamine and pilocarpine were also given, and though each appeared to have a slight stimulative action, the extent of the response usually was not greater than the normal.

COMMENT

We have already enumerated the chief methods that are employed to investigate the intestinal motor response to various drugs, extracts and other therapeutic agents. In each it is easy to find when error is introduced, so that the employment of a new method, even though it does introduce new difficulties, is more or less justified so long as it overcomes some of the old pitfalls. And not only may it enable

Even before there is any visible deposit of calcium salts, the matrix of this trabecular network stains more deeply than the adjacent cartilage. The beginning of calcification in this region can be seen, and occurs as a deposition of small granules which appear first around the periphery of the lacunae of the cartilage cells. The thin layer of matrix forming the actual capsular wall of the lacunae is always clear of granules. The deposit increases and spreads in the matrix until the latter is completely filled with closely packed granules, which become almost a solid mass.

Calcification of Cartilage in Epiphyses of Long Bones.—The calcification of the cartilage of an epiphysis and its later ossification are initiated in the center of the mass. Before its appearance blood vessels are found in the epiphysis (figs. 2 and 3, plate I), invading it from various surfaces and branching within it so as to enclose a small central area within which are initiated all the changes terminating in its conversion into bone. Included among the vessels are some which penetrate the epiphyseal plate and enter the epiphysis from the end of the shaft of the bone. In all respects the epiphysis develops as though it were an independent bone, and the process is exactly similar to that found in the short, irregular bones such as the tarsals and carpals next described, so that the epiphyses should evidently be included in this next class.

Calcification of Cartilage in Short, Irregular Bones.—In the epiphyses of the long bones and in such bones as the carpals and the tarsals, there are some interesting differences from the process of development seen in the shaft of the long bone. The navicular, cuboid, talus and calcaneus of older fetuses and new-born children provide particularly good specimens for examination, giving all stages from solid, unchanged cartilage to complete calcification and the formation of true bone.

In these cases it was learned that blood vessels enter the cartilage and ramify in it for long periods, sometimes for many months (fig. 4, plate II), before the changes begin which accomplish ossification. In spite of their presence, the cartilage remains unchanged. The vessels enter from all surfaces except those articulating with other elements of the skeleton and penetrate to a zone about midway to the center, where they branch and run parallel to the surface, anastomosing freely. This vascular zone thus surrounds a solid central core of cartilage, the surface of which in contact with the vessels will be the exact external surface of the future calcified center of the developing bone.

Some time before the center of ossification is due to appear, changes occur in the cartilage preparatory in character to this event. There is first noticed a marked augmentation in the size of the cartilage cells in the region of the vessels and just proximal to them toward the center of the mass. Accompanying this change is a great increase in the amount of matrix between cells, and this matrix stains poorly and is pale.

us to get new ideas and conceptions about an old and long studied condition, but it may also serve to show how remedial agents affect that condition when their action is investigated in a new light. Therefore, the introduction of a new method of study, we feel, is justified in order that its efficacy may be tested and the results of previous studies confirmed or disproved.

In the main, this means of determining the action of various drugs on intestinal musculature does away with those difficulties that arise in the experiments on isolated muscles, such as temperature, acid-base equilibrium and nutritional factors. The drug that is added to the medium in which the isolated slip of muscle is suspended comes in contact with the muscle through a different path from that which approaches it through the blood stream. There is no interference with any of the local or general nervous mechanisms, while all those systems and structures such as blood pressure, through which a drug may exert its influence primarily or secondarily, are intact. In a moderate degree, too, a measure of the degree of the activity of a drug or extract may be gaged by its influence on the intra-intestinal pressure which is afforded a constant graphic representation. A repeated number of observations can also be made on the same animal. Of course, it must be borne in mind that each experiment is made on a dog that is in a pathologic state which each day becomes more severe, leading to a lowered resistance, gross changes in the blood chemistry and probable metabolic disturbances. These are comparable, however, to the same conditions that exist in human beings when the need for intestinal stimulants is paramount. So that the measures employed to prepare the animal for experimental purposes, and the early and late sequelae that result therefrom, do not introduce so great a degree of error as they would appear to do at first. A further point to be considered when comparing experiments on isolated tissue with those on the intact animal is that in the latter case the normal channels are present which influence the destruction or excretion of the drug.

A final interesting observation noted during these studies was the cause of death in one dog that was given repeated doses of eserine. While, for the most part, the animals would die from a complicating peritonitis resulting from a leak about the apparatus, in this dog, which received large and repeated doses of eserine that raised the intra-intestinal pressure greatly above what it would have been had this drug not been employed, the cause of death was from a perforation of the intestine. In this animal the small intestine was greatly distended for many inches above the site of obstruction; the antimesenteric border exhibited large diamond-shaped ecchymotic areas, ulceration of the mucous membrane and a fair sized perforation. A similar condition was not found in those animals to which eserine was not given. Indeed,

Immediately internal to the level of the blood vessels the cartilage cells now become irregularly grouped, not in columns as in the long bones but in clumps and small masses. Between these occur strips of matrix which do not contain cells, and which branch and intercommunicate and are destined to form the persisting cartilaginous network of trabeculae on which in later stages the first bone will be deposited. These trabecular areas give early indication of their future destiny (fig. 4, plate II; fig. 7, plate III, and fig. 10, plate IV) by staining more deeply than the remainder of the matrix and by being the first portion of the cartilage to become calcified. In later stages of development, it was quite noticeable that this intermediate trabecular zone adjacent to the blood vessels was completely calcified (figs. 5, 6 and 8), while the center of the mass still contained little if any calcium. Sections of a bone at this stage showed that there was a central region not yet calcified surrounded by a completely calcified layer; this again was surrounded by a ring of blood vessels and finally by a zone of unaltered cartilage on the exterior.

The first appearance of the deposition of calcium in these cartilages in every case was in the form of fine granules (fig. 11, plate IV) deeply stained with hematoxylin, lying in the matrix immediately outside the capsule of the cartilage cells, and always occurring first around those enlarged cells lying closest to the blood vessels. The primary zone of calcification is thus in the area of enlarged cartilage cells just internal or proximal to the blood vessels, and forms the calcified surface of a sphere (figs. 5 and 6, plate II), the center of which gradually calcifies later. This condition was extremely well shown in one talus which to the naked eye appeared completely calcified except for a thin external shell of unchanged cartilage, and which cut with some difficulty with the knife. In this specimen it was found, however, that cartilaginous trabeculae in the center of the area contained little if any calcium, although this was a later stage in calcification and the region was invaded by blood vessels and was full of primary marrow cavities, with beginning ossification of the area.

Blood vessels do not invade the central portion of the cartilage until it begins to calcify, but when once this process has taken place they erode and penetrate the periphery of the calcified mass (figs. 5 and 6, plate II) at various places and expand and anastomose within it, eroding large portions to form the primary marrow cavities. These are formed simultaneously with the occurrence of true ossification, which is now initiated with the deposition of bone by the osteoblasts on those calcified cartilaginous trabeculae which are not eroded. From this point onward, ossification advances toward the surface of the bone by growth on the

it is a rare occurrence in those dogs that die from simple intestinal obstruction to find at autopsy a perforation of the intestine at the antimesenteric border.

In discussing the results obtained from the use of pituitary fluid and pituitrin, we must admit that we found these different from what we had expected, though on more careful examination of the literature, not unlike those which other investigators had reported. When one observes in one place that solution of pituitary is a stimulant of smooth muscle and in another that it relaxes a suspended slip of small intestine, the only conclusion to be drawn is that either a different extract was employed in each case or the methods of observation introduced differences that in the end resulted in different conclusions. So far as the action of the extract on the isolated muscle is concerned, a great deal has been done to show the error that is introduced by depressor substances common to many tissue extracts, and also preservatives employed in the commercial products. Changes in the P_H of the bath as a cause of relaxation of strips of intestine have recently been emphasized by Gruber.³⁶

The constancy of results that we have obtained, however, associated with the constant constitutional effects that have followed the giving of pituitary fluid, intramuscularly and intravenously, convinces us that they are true. Special precautions were taken to free the powder from which the fluid was made of all depressor substances, and a preservative was not added.

A word or two must be said about the change in the intra-intestinal pressure that is shown in table 1 under maximal pressures before and after injection. As a general rule, it is seen that the pressure in the column headed "Before" shows a greater pressure than that headed "After." The interpretation of this is that just before the injection of the pituitary fluid a period of increased intestinal pressure occurred, while after the injection the pressure fell off, and the intestine was apparently inactive until the effects of the extract had worn off. In some other instances, the pressure before the injection is not greater than after it. In these cases the intestine was apparently inactive for the few minutes immediately preceding the giving of the pituitary fluid, and no stimulation resulted with the exception of a continuation of inactivity and generally a falling off of the tone. Occasionally, a great degree of pressure is noted just before the injection. In these instances eserine had been given, and while it was still active, pituitary fluid was administered, which resulted in an abrupt fall of pressure.

So far as we could determine, there was no change in the degree of activity of the intestinal musculature following injections of pituitary

36. Gruber: *J. Pharmacol. & Exper. Therap.* 30:73, 1926.

PLATE II

Fig. 4.—Horizontal section of a cuboid in a seven months human fetus. This bone ossifies in the ninth month but already there is a pale central area surrounded by one containing a network of darkly stained trabeculae lying just within the zone of blood vessels; $\times 8$.

Figs. 5 and 6.—Sections of the talus (astragalus) of a seven months human fetus. The center of ossification occurs in this bone in the seventh month and is shown in the illustrations. It is really the center of calcification of the cartilage at this stage, and true ossification is just beginning to occur in it, coincident with its penetration by the blood vessels which are shown entering it; $\times 8$.

fluid so far as a relationship to the duration of the obstruction was concerned. The response in a dog in which obstruction for forty-eight hours was produced was the same as that in one obstructed six or seven days. In the same way, when a terminal peritonitis set in, a change in the usual response could not be observed.

The changes in the intra-intestinal pressure were observed for from one to two hours after the giving of the pituitary fluid. After from thirty to forty-five minutes, the changes in the pulse rate and the degree of pallor of the mucous membranes would have returned to normal. The rhythmic intestinal activity would also ensue in from twenty to forty minutes as a general rule, but a degree of activity or a rise in the intra-intestinal pressure that was greater than it had been before the administration of the pituitary fluid was never observed.

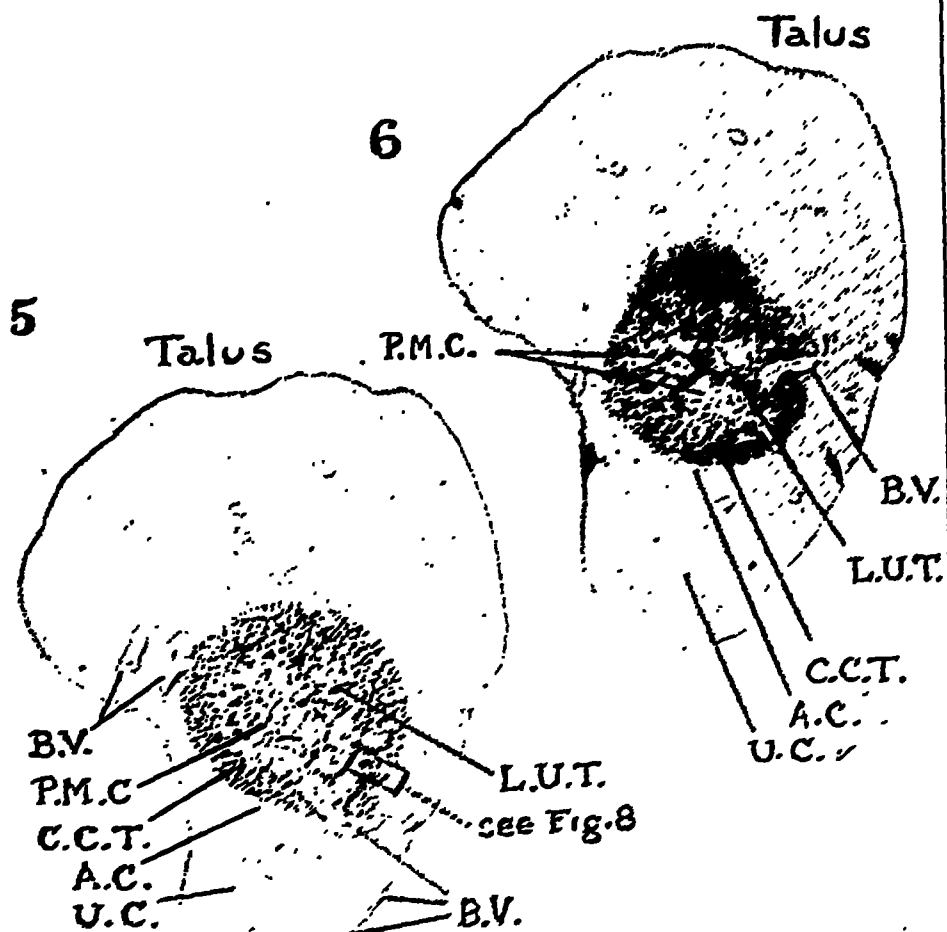
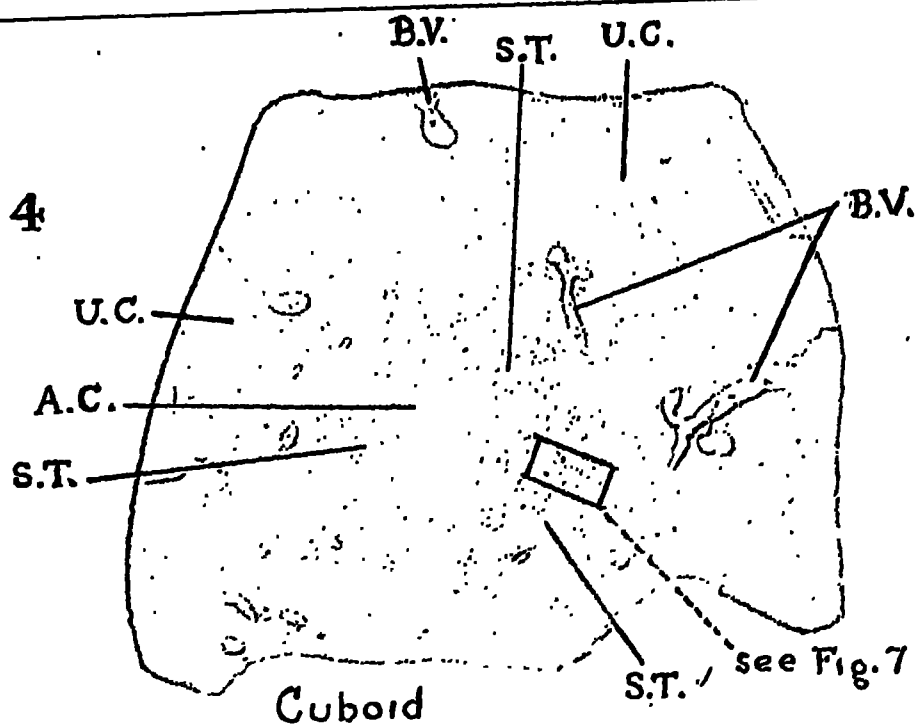
It must be stated that we have no record of the action of the solution of pituitary on the large bowel, nor have we any for the experiments on the isolated intestine. It is just possible that there might be a somewhat different response in this portion of the intestinal canal which would account for the defecation observed by some investigators following the injection of solution of pituitary.

An exact explanation of how this tissue fluid acts on the intestinal canal to bring about the results just stated is rather difficult. It would appear reasonable, however, to assume that, as the action of pituitary fluid on the isolated slip of intestine was no stimulation, a fall in tone or a cessation of rhythmic movements, while in the animal there was always a cessation of movement without exception, probably besides a possible direct action on the muscle itself; there was also a second factor, possibly the anemia of the wall of the bowel due to a vasoconstriction, or some other secondary effect.

While the use of pituitary solution is strongly advocated in all cases of intestinal paresis, it has by no means a constant and adequate therapeutic value. The opinion of various clinicians might vary so far as this point is concerned, but in the light of our studies, we should not expect a return of or an increase in the peristaltic activity following the use of the pituitary fluid we have employed.

In our experience, eserine was the most effective intestinal stimulant. Both in the response of isolated intestinal muscle to this drug and in all instances in which a sufficient dosage was given to the living animal, there was observed, as was previously stated, not only a rise in the tone of the bowel, but also a great increase in the degree of motor activity.

Hypertonic sodium chloride, too, would appear to increase the intestinal motor function. We are unable to state whether the extent of this action is greater when the blood chlorides have fallen to below normal, but we do feel that the stimulative power is greater late in the



obstruction. Reference should be made here to the work of Haden and Orr,³⁷ who stated that ligation of the dog's ileum at the ileocecal valve is followed by little increase in the nonprotein nitrogen of the blood, no change in the blood chlorides and carbon dioxide combining power of the plasma. This being the case, then, the value and efficacy of hypertonic sodium chloride as an intestinal stimulant would not bear any relation to the percentage composition of the chlorides in the blood.

SUMMARY

1. A method of recording the movements of the small intestine and the degree of intra-intestinal pressure in simple intestinal obstruction in dogs is described.

2. The effect of various solutions of pituitary and certain drugs on the movements of the small intestine and the intra-intestinal pressure in obstruction is recorded.

3. The action of pituitary fluid, pituitary, vasopressin and oxytocin on the obstructed intestine would appear to be one of depression and slight relaxation, though the general or other systemic effects induced by these extracts may vary considerably.

4. On the isolated portion of dog's intestine, whether from normal or obstructed bowel, the effects of pituitary fluid and pituitary are those of relaxation if any change occurs.

5. In the dog with intestinal obstruction, intramuscular injections of eserine in adequate amount have a decided stimulative action on the small intestine. The rise in the intra-intestinal pressure is also great and may measure more than 100 cm. of water.

6. The value of hypertonic sodium chloride as an activator of peristalsis is proved experimentally.

37. Haden and Orr: *J. Exper. Med.* 37:365, 1923.

periphery of this central mass in the same way that it extends toward the ends of a long bone.

It will be seen that in all essential features calcification and ossification follow the same process in bones such as the tarsals as that followed in the long bones. The noticeable differences shown in the tarsal bones are: first, the early presence of blood vessels in the cartilage, long before the appearance of the centers of calcification and ossification; second, the appearance of calcium in the matrix at several places simultaneously to mark out a periphery for the region in which the alterations are occurring; third, the lateness of the occurrence of budding of the blood vessels and their formation of primary marrow cavities in the mass; fourth, the reversal of the direction of growth of the calcified area, which grows toward the entering blood vessels and not away from them as in the long bones.

Calcification of Cartilage in Bones of the Skull.—The development of the cartilage bones of the skull is similar in process to that in the rest of the skeleton and need not be described in detail. One point worthy of note, however, is the fact that calcification (fig. 9, plate III) may occur without any blood vessels being present in the cartilage.

In the skulls of young human embryos in which the cartilaginous rudiment of the future bones is not thick, it does not seem essential for their nutrition that blood vessels should be present in them. Preparatory to calcification, the matrix shows poor staining qualities and the cartilage cells enlarge as in other bones. The enlargement of the cartilage cells progresses until they are crowded one against another with a thin lattice or network of matrix between. At this stage, calcification of the matrix occurs by deposition of the calcium salts as granules in it. These granules are seen first immediately outside the circumference of the cells, and gradually those of contiguous cells merge to fill and make solid the partitions between adjacent cells. This obviously looks as though the placing of the granules was due to cellular activity.

Ossification follows this stage by the deposition of true bone subperiosteally on the calcified cartilage, and later this cartilaginous core to the future bone is gradually removed and replaced by true bone.

II. PHYSIOLOGIC CALCIFICATION DURING OSSIFICATION.

Here two somewhat different conditions, due to the difference in origin of the bones developed in cartilage or in membrane, are considered.

Ossification of Membrane Bones.—In membrane bones the development was seen clearly in serial sections of the heads of young human embryos, the parietal bones and mandibles furnishing particularly good examples.

be given and also an intracardiac injection of 1 : 1,000 solution of epinephrine hydrochloride or 1 per cent solution of ephedrine must be administered. One cubic centimeter has been used with good results.

For artificial respiration, compressed air, which is forced into the lungs through a tin mask, has been used. The tubing is so arranged that either air alone or air saturated with ether can be given. If a varying degree and length of pressure on the floor of the mouth is applied in the dog, the amount and also the pressure of the air that is introduced into the lung can be regulated. The length and the degree of compression must be such that the lung distends to its full capacity in the open chest.

RESULTS

Fifty-four partial or complete pneumectomies were performed on dogs. Nine of these animals died on the table during the earlier period of the experiments. As my associates and I became more expert in technic and as accidents and emergencies were watched for, the point was reached where the dogs survived the effects of the operation and lived for a long time. Of the nine that died on the table, six died of asphyxia caused by unsatisfactory artificial respiration. One dog died as a result of an accidental acute hemorrhage from the pulmonary artery. This hemorrhage resulted from the premature release of the compressing clamp at the hilum. The clamp could not be easily reapplied, and by the time it was reinserted the dog was exsanguinated. Digital pressure was not thought of until it was too late. Two other dogs died as a result of an acute dilatation of the stomach. This dilatation was encountered frequently, but two dogs were killed before it was found that a prompt emptying of the stomach with a tube was all that was needed. Another factor that shortened the postoperative life of the animals was distemper. Nine dogs developed this disease, and all died as a result.

All of the dogs showed evidences of pleural irritation with a greater or lesser amount of exudation. In those that died during the first ten days the chest was found full of serosanguineous exudate which would not clot either in or outside of the chest. Such a fluid was present on both sides. I believe that the fluid found its way into the opposite side through the thin mediastinum of the dog. Such has been my experience when fresh blood was injected into one side of the thorax. When the animal was killed two days later, the blood was present in about equal amounts on both sides. The site of suture was always found to be adherent to the wall of the chest and generally at the site of the thoracotomy. In the first ten days, the adhesions were fibrinous or a weak fibrous type. As the interval became longer the adhesions became stronger, so that in some cases the stump could be separated from the wall only by means of a sharp dissection (fig. 2).

Infection and leakage were encountered in one stump. In this experiment, an undue amount of strength was used to tie the suture and thus necrosis and a slough were caused.

During the first week the stump was dark purple and presented little crepitation. During this period, areas of hemorrhage into the interstitial tissue and the alveolar spaces were seen microscopically. At the site of the suture, the alveolar spaces were compressed in one direction and then were changed into strands of tissue (figs. 3 and 4). The bronchiol

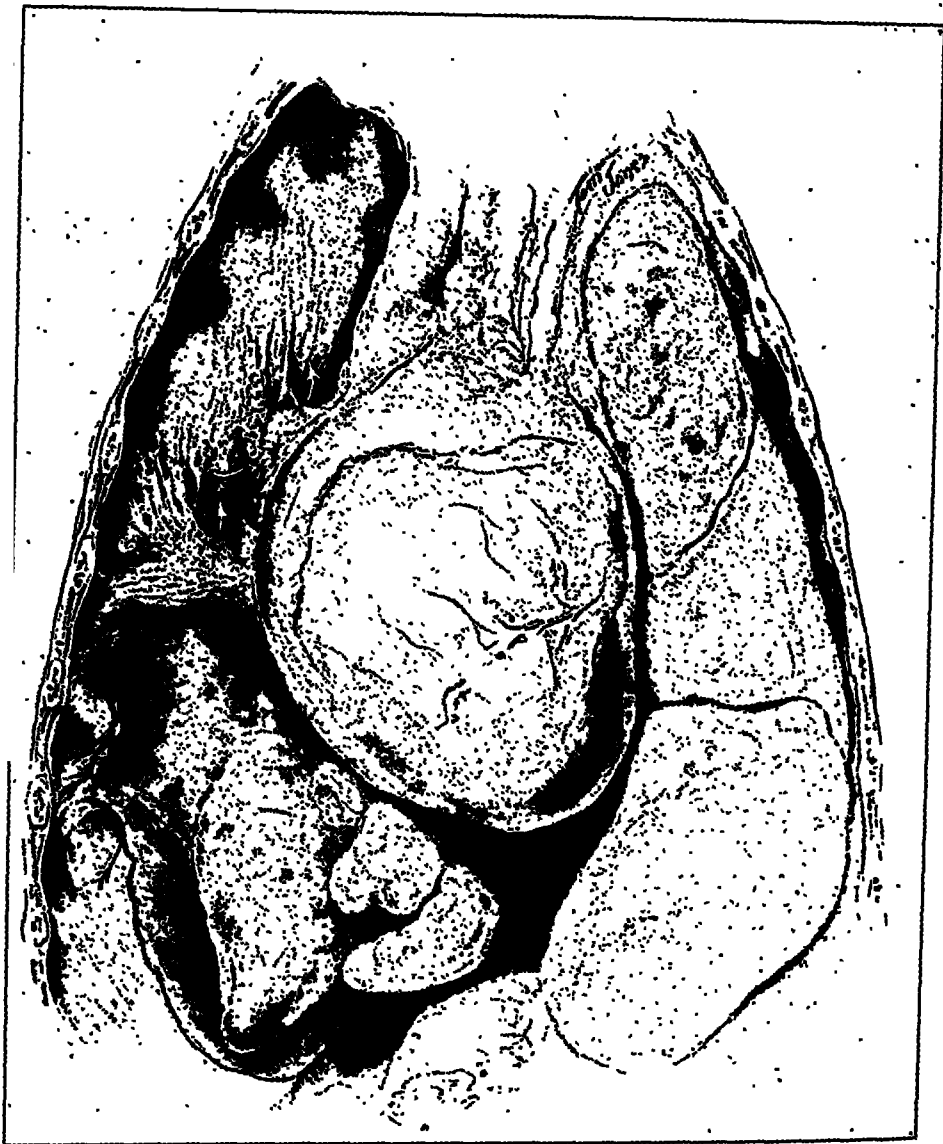


Fig. 2.—Appearance of the stump thirty-two days after an upper right lobectomy with the author's technic. The scar tissue binding the stump to the wall of the chest and pulling the mediastinum to the right side should be noted. The arrow points out the communications above and below the stump. Pathologic

The matrix of the osseous tissue is of a fibrous nature. In the fibrous membrane which precedes those bones developed in this manner, there is a ground substance which is already prepared for impregnation with calcium salts in a permanent form. The deposition of calcium salts starts on the surface of the membrane while it is still thin. Here a layer of cells under the sheath and in relation to a fairly good blood supply begins to impregnate the fibrous tissue on which they lie with a fine granular deposit. This occurs first in contact with the periphery of that side of the cell in relation to the membrane. As the cell becomes embedded deeper and deeper in the new bone which is being formed, the granules are found extending farther around the cell until finally it is entirely enclosed in a calcified matrix and is now a bone corpuscle as distinguished from an osteoblast. In stained sections, the granules form a dark border outlining the cells.

It is almost universally believed that the bone forming cells here exude the fibrous organic matrix, and from my studies I believe that the calcium salts are also exuded into this matrix or simultaneously with the matrix, where they then crystallize out or precipitate to give the bone its strength and hardness.

Ossification of Bones Developed in Cartilage.—In bones developed in cartilage, there is no matrix ready for permanent impregnation with calcium. The cartilage lying in any zone about to be ossified becomes calcified, but much of this is immediately removed by erosion and absorption. What remains is merely a temporary scaffolding to support the true bone which is first laid down on it and covers it. When the quantity of bone becomes sufficient for its own support, even this part of the cartilage is finally removed.

The bone which is first formed is deposited as a thin layer on the surface of the trabeculae formed of calcified cartilage. It is deposited by the secretory activity of the osteoblasts, which exude the organic matrix and simultaneously seem to pass the calcium salts into it. These salts first become visible in the matrix in an extremely fine granular form, the granules being much more minute than those seen in calcified cartilage. Whether the calcium salts become solid by a process of crystallization out of the solution or a process of precipitation is not known. I believe that their presence in the matrix is, however, due to the secretory function of the osteoblast in placing them in this position.

NORMAL CALCIFICATIONS

In the previous part of the paper, the facts as gleaned from my investigations of the development of the skeleton have been presented. It remains now to review these and to state the conclusions to which one may be led by them.

His conclusion is that faulty utilization of bone forming elements in rickets is due to defective absorption and that this in turn depends on a change in gastro-intestinal conditions.

Wilkins and Kramer¹³ proved that the beneficial effect of cod liver oil on rickets could be obtained by an ether soluble extract injected intramuscularly, showing that the effect is a general one exerted through the circulation and not a local one simply due to the presence of the oil in the intestine. Flamini¹⁴ showed that the antirachitic vitamin in cod liver oil increases the absorption of calcium from the intestine and aids in its fixation in the tissues.

In spite of their lower concentration in the blood of rachitic individuals the calcium salts are present in a supersaturated solution, according to Holt, La Mer and Chown,¹⁵ and so the failure of the salts to be deposited in the bones must be due to more than a simple lack of precipitation.

Beckhold stated that precipitation of calcium is hindered by the colloids in the blood, and this hindrance must be prevented during ossification, the protective action of the colloids being changed at or by the bone cells. He also noted that Witte's peptone holds only calcium carbonate in solution, while calcium phosphate precipitates out of it. In this he saw the explanation of why there is so much more phosphate than carbonate in bone, because peptones are formed as the cartilage breaks down ahead of the ossification. In rickets there is an overgrowth of cartilage with less breaking down and, consequently, a smaller deposition of calcium salts and a softer bone.

Further evidence of the part played by the cell in the deposition of calcium in bone and cartilage is seen in the work of Robison, Kay, Soames and others.¹⁶ They demonstrated that those tissues which utilize phosphates all possess a ferment called phosphatase, or esterase,

13. Wilkins, L., and Kramer, B.: *Infantile Rickets: Treatment by Intramuscular Injection of a Cod Liver Oil Concentrate*, Bull. Johns Hopkins Hosp. 40:52, 1927.

14. Flamini, Mario: *The Action of the Antirachitic Vitamin of Cod Liver Oil on the Organism of the Child*, *Pediatrics* 34:625, 1926 (*Child Devel. Abstr.*).

15. Holt, L. E.; La Mer, V. K., and Chown, H. B.: *Studies in Calcification: I, II and III*, J. Biol. Chem. 64:509, 1925.

16. Robison, R.: *The Possible Significance of Hexosephosphoric Esters in Ossification: I*, *Biochem. J.* 17:286, 1923. Robison, R., and Soames, K. M.: *The Phosphoric Esterase of Ossifying Cartilage*, *Biochem. J.* 18:740, 1924. Kay, H. D., and Robison, R.: *The Action of the Bone Enzyme on the Organic Phosphorus Compounds in Blood*, *Biochem. J.* 18:755, 1924. Goodwin, H. W., and Robison, R.: *Phosphoric Esters of the Blood*, *Biochem. J.* 18:1161, 1924. Martland, M., and Robison, R.: *The Enzyme in the Early Stages of Bone Development*, *Biochem. J.* 18:1354, 1924. Robison, R., and Soames, K. M.: *A Chemical Study of Defective Ossification in Rachitic Animals*, *Biochem. J.* 19:153, 1925. Kay, H. D.: *Kidney Phosphatase*, *Biochem. J.* 20:791, 1926; *The Function of a Phosphatase in Bone Formation*, *Brit. J. Exper. Path.* 7:177, 1926.

PLATE III

Fig. 7.—Photomicrograph of the area outlined on cuboid in figure 4. The arrow points to the center of the bone. Note the darkly staining trabeculae, although a visible deposit of calcium salts cannot be identified; $\times 150$.

Fig. 8.—Photomicrograph of the area outlined on talus in figure 5. The arrow points to the center of the bone. The cartilage cells are grouped in columns lying radially, and the dense black areas are the heavily calcified areas formed of closely packed granules. The granules are not visible in the photograph owing to the thickness of the section and the density of the stain taken by them; $\times 150$.

Fig. 9.—Photomicrograph of a portion of the base of the cranium of a human embryo 43 mm. long. The heavy black areas between cartilage cells in the center of the section are calcified areas densely stained. Blood vessels are not present in this cartilage; $\times 150$.

which will produce inorganic, ionizable phosphates from organic phosphoric esters. The phosphatase varies with the animal, the tissue and the age; it will stand considerable heat and can be kept for months and will still remain active.

Kidney phosphatase will hydrolyze all the acid-soluble phosphates in the blood, while bone phosphatase will hydrolyze only part of them. Bone phosphatase is not present before the beginning of ossification or in the cartilaginous ends; it is present in quantity in all bone, even in old age and is in maximum amount in the ossifying zones during growth and is coincident with and in proportion to the amount and rapidity of growth.

Eden¹⁷ found large amounts of calcium in the callus of healing fractures, which were transparent on roentgenographic examination. The calcium was evident here in a form bound to the protein of the callus. He also made injections of solutions of calcium salts into the site of fracture and obtained much more rapid healing, showing the effect of a good supply of calcium on cellular activity.

Rabl² said that the calcium in growing bones is to be found in a form bound to peptids and amino-acids formed by the breaking down of the cartilage in the region. Carbonates are produced through the liberation of carbon dioxide on further decomposition and the phosphates precipitate by reaction with soluble phosphates of the tissue fluids. One might see here the use of the esterase previously mentioned in increasing the amount of available phosphates.

The problem raised here does not yet appear capable of solution, but consideration of the facts leads to the assumption that the cell must have considerable influence on the deposition of calcium salts in cartilage. The weight of evidence, one feels, is in favor of the view that the cartilage cell has some secretory activity, the exact process of which is as yet unknown, which is accountable for placing the calcium in the matrix.

This view is similar to the one I have already advanced that the calcium contained in the matrix of the bone is deposited by secretory activity of the osteoblasts and bone corpuscles, and my reasons for inclining to this view have been fully set forth in previous papers.¹⁸

The deposition of calcium in bones developed in membrane, being in the form of fine granules immediately surrounding the osteoblasts

17. Eden, R.: Untersuchungen über Vorgänge bei der Verknöcherung, *Klin. Wchnschr.* 2:1798, 1923.

18. Watt, J. C.: The Behaviour of Calcium Phosphate and Calcium Carbonate (Bone Salts) Precipitated in Various Media, with Applications to Bone Formation, *Biol. Bull.* 44:280 (June) 1923; The Deposition of Calcium Phosphate and Calcium Carbonate in Bone and in Areas of Calcification, *Arch. Surg.* 10:983 (May) 1925; The Transport and Deposition of Calcium Salts in the Body, *M. J. Australia* 2:85 (July) 1925.



PLATE III

(which also form the bone corpuscles when fully embedded), is in all essentials similar to the process of calcification of cartilage, and its consideration leads to similar conclusions.

It is interesting to note in this regard that Weidenreich¹⁹ published two comprehensive articles on the constitution of bone, in which he described three divisions of this tissue: fiber bone, cartilage bone and lamellar bone. He considered the lamellar bone of the haversian systems as being the only true organized bone tissue, with true bone corpuscles and with a finely granular calcium content to its matrix, which may be even homogeneous from fusion of the deposits into a mass.

Fiber bone is regarded as simply a dense calcification of fibrous tissue; it is found as the subperiosteal deposit on the surface of all bones, in muscular prominences of the skeleton and in all the bones formed in membrane. It can also be seen in ossified tendons. The deposit of calcium here is in a much coarser granular form.

Cartilage bone is seen in the early embryonic ossifications and also in the calcification of certain epiphyses, especially those occurring late, and contains calcium in a coarse granular form.

The two latter forms of bone appear in the embryo and also during later growth as the kind of bone which is formed first in any location. Much of this material is later reorganized and converted into the lamellar type by activity within the bone. What I have found true, especially concerning the physical state of the calcium salts in various bones, is in perfect accord with Weidenreich's statement.

Two other instances of normal calcification which may be considered are the formation of the shell in the hen's egg and the shell of the fresh water clam. Both of these structures are regarded as products of secretion. The clam shell is considered due to the secretion of calcium carbonate in albumin on the surface of the animal's mantle. This salt, as Pauli and Samec²⁰ showed, is seven times as soluble in albumin as in water and so can be secreted in appreciable quantity. The solubility is also increased by the carbon dioxide content of the tissues. When the secretion is exuded on the surface of the mantle, the lowered carbon dioxide content of the water causes the calcium carbonate to precipitate. Being in a colloidal solution it separates out in the colloidal form of deposit, which is usually small spherules; these have a marked

19. Weidenreich, F.: Knochenstudien: I. Ueber Aufbau und Entwicklung des Knochens und den Character des Knochengewebes. II. Ueber Sehnenverknöcherungen und Factoren der Knochenbildung, *Ztschr. f. Anat. u. Entwicklungsgeschichte*, 69:382 and 558, 1923; Ueber den Begriff "Knochen" und die Beziehungen des Knochengewebes zu Bindegewebe und Knorpel, *Anat. Anz.* 57:138, 1923.

20. Pauli, W., and Samec, M.: Ueber Löslichkeitsbeeinflussung von Electrolyten durch Eiweisskörper, *Biochem. Ztschr.* 17:235, 1909.

In the case of those bones which are preformed in cartilage, it may be stated that calcification of the cartilage occurs in all cases previous to ossification. The calcified cartilage is not transformed directly into bone but is removed. Much of it is immediately absorbed, while the remainder, forming a scaffolding of trabeculae for the support of the bone which is first produced, is later absorbed, when the true bone is formed in sufficient amount to support the skeleton.

The cartilage may go through all the changes ending in calcification, without the presence of any blood vessels (fig. 9, plate III) in it if it is small or thin, as may be seen in the case of some bones of the skull. But if the cartilage is of larger mass (fig. 2, plate I and fig. 4, plate II), then blood vessels will be present in it. However, they will stop just short of, and will not ramify in the calcified area itself until that moment (figs. 5 and 6, plate II) when the area is invaded by the budding blood vessels carrying in the osteoblasts to initiate true ossification.

An interesting view has been suggested to me to explain the presence of a skeleton formed of calcified cartilage in the embryo. It will be recalled that in the lowest forms among the vertebrates the skeleton is not true bone but is only a calcified cartilage. The bony skeleton first appears in the higher fishes, replacing a cartilaginous one. Thus the temporary appearance of a calcified cartilaginous skeleton for a short time just previous to the appearance of the permanent bony skeleton in the embryo of all higher vertebrates is to be interpreted as an evolutionary phenomenon, reflecting the past history of the race. It is a case of phylogeny being repeated in ontogeny in the skeleton in a way similar to that seen in the case of the kidney. In the latter, there is the succession of pronephros, mesonephros and metanephros as excretory organs, only the last persisting as a kidney in the highest vertebrates. In the skeleton one finds the succession of cartilage, then calcified cartilage and finally bone.

The calcifying of the cartilage, which is thus so temporary and transient, appears to serve a practical purpose in the embryo by providing a large amount of calcium ready for use by the osteoblasts in the first rapid formation of bone.

In those bones developed in membrane, the organic matrix necessary to receive the calcium salts is already present and does not need to be altered, as was the case with the cartilage, so the more permanent deposition of salts is made directly into this fibrous matrix. The latter is similar to the new matrix that is formed by the osteoblasts which produce bone in a cartilaginous area. The method of bone formation in membrane is therefore much like a calcification of fibrous tissue, with this difference, however, that the calcium salts appear in intimate relation with the characteristic tissue cells, namely, the osteoblasts and bone

tendency to fuse and so produce the dense pearl shell. The contact of the water with the albuminous solution no doubt aids in the precipitation also by its tendency to dilute the albumin and so render the contained calcium salt less soluble.

The process of formation of the clam shell is thus seen to be a double process. There first occurs secretion of the calcium carbonate in a soluble form in an albuminous matrix through the agency of the mantle cells. Secondly, there is a precipitation and fixation of this secretion by physical and chemical means, through which the calcium carbonate combined with the albumin in colloidal crystals is deposited. That albumin combines with the crystals was shown previously as far back as Rainey's²¹ period by decalcifying experimental precipitates and obtaining perfect albuminous casts of the deposits after the calcium is removed.

A second example of the secretion of calcium is to be found in the formation of the shell of a bird's egg. The shell is composed almost entirely of calcium salts and is secreted by the shell gland, a modified part of the genital tract, and an evident and undeniable cellular activity is concerned here in the output of calcium. The final deposition in solid form about the egg may again be a precipitation due to the concentration of carbon dioxide found in the genital passage which is lower than the concentration existing in the tissues. But the placing of the calcium here where it can precipitate is certainly due to the secretory work of the mucosa of the shell gland in taking the calcium salts from the blood stream and passing them through to its free surface.

In the case of the formation of the teeth, the manner in which calcium is deposited again comes into question. There is a definite organic matrix to both the enamel and the dentine, laid down, respectively, by the ameloblasts and the odontoblasts.

In the matrix of each layer, the calcium is found deposited in the form of minute granules. These were interpreted by Rainey, and by others since his time, as indicating their production by precipitation, as they are exactly of the form and appearance seen in experimental precipitation of calcium carbonate in colloids. But the inorganic material of the teeth is largely calcium phosphate, which has been shown (Rainey,

21. Rainey, G.: On the Formation of the Skeletons of Animals, and Other Hard Structures Formed in Connection with Living Tissues, *Brit. & Foreign Med. Chir. Rev.* 40:343, 1857; Precise Directions for Making of Artificial Calculi with Some Observations on Molecular Coalescence, *Quart. J. Micr. Sc.* 6:41, 1858; On the Structure and Mode of Formation of the Dental Tissues, According to the Principle of Molecular Coalescence, *Quart. J. Micr. Sc.* 7:212, 1859; Some Further Experiments and Observations on the Mode of Formation and Coalescence of Carbonate of Lime Globules, and the Development of Shell Tissues, *Quart. J. Micr. Sc.* 1:23, 1861.

corpuscles. The development of bone in membrane is, of course, also phylogenetically significant, for it, too, repeats the history of development of this type of bone.

In all cases of calcification of cartilage observed, the following facts are to be noted:

1. The calcium salts always appear first in the form of granules.
2. These granules appear first around the cartilage cell (fig. 11, plate IV) and are embedded in the matrix immediately outside of the cell capsule.
3. The salts appear before blood vessels are present in the calcified areas.
4. The calcium salts do not appear until after changes have occurred both in the cartilage cells (fig. 4, plate II; fig. 7, plate III, and fig. 10, plate IV) and in the matrix of the area to be calcified. The cells become grouped and greatly enlarged; the matrix increases considerably, becomes pale and stains poorly.

It thus appears that the association of calcium deposits with the cartilage cells is close and that the whole manner in which calcification occurs leads to the conclusion that the cell has considerable control of it, and that the calcium arrives in the matrix somehow as a result of the cell's activity.

According to all investigators, precipitation of calcium salts in solution in the body tissues occurs when the carbon dioxide content is lowered. It seems reasonable to infer that the matrix farthest away from the cells in the cartilage would contain the least carbon dioxide which, being a product of the activities of the cells, should be most concentrated in its immediate neighborhood. If this inference is correct, the first place in which calcium salts would be deposited would be in the larger masses of matrix and as remote as possible from surrounding cells. This is not the case, but the opposite is true. The first deposition is immediately surrounding the cell capsule, so that the granules evidently do not occur by precipitation from decrease of carbon dioxide in the cartilage.

The view has been put forth that calcium salts are precipitated as carbonate and phosphate by the reaction of these radicles excreted by the cells uniting with calcium dissolved in the fluids of the matrix. If this were so, one would expect the deposition to be equal all about the circumference of the cell, but in the early stages of calcification the deposit is frequently found lying all to one side of the cartilage cell, although there was plenty of opportunity for it to be surrounded completely.

Harting,²² Watt) to precipitate even in colloids as an extremely fine granular suspension. Only the carbonate forms globules and spherules, so that the constant appearance of the calcium phosphate in the teeth in globular form is not to be interpreted without question as indicating a simple precipitation.

The problem as to how the calcium actually deposits in the enamel or the dentine of a tooth is underlaid by a still more fundamental problem as to how the calcium salts are brought into this region where they are later laid down. If they simply diffuse into the matrix, then the whole process of deposition is a simple precipitation. But if they are selected and passed into the region by cellular activity and then appear as a solid deposit, it is evident that although the end of the process may still be a precipitation, nevertheless, the beginning is a vital process, secretion by the cells forming this tissue. This is an important and far reaching difference and is of great significance in understanding the development of the teeth; it will modify radically all attempts to treat abnormal conditions such as defective calcification.

Concerning the teeth, Blotevogel²³ did work which is of great significance. He made injections of trypan blue into young mice and then examined the developing teeth at intervals of from one to thirty days. He found that the ameloblasts, which form the enamel, and the odontoblasts, which produce the dentine, both stored the vital dye evenly throughout the cell before they became active. But when they began to form the enamel and dentine, both these types of cells showed marked polarity, with a definite direction of transport of material through the cell. This was shown by the fact that all granules became closely packed along that edge of the cell which was forming the enamel or the dentine. The organic matrix of the enamel or dentine formed during the period when the dye was present was also colored diffusely blue.

When the enamel and dentine became calcified the parts which contained calcium were colorless, either because the calcium does not combine with the dye or because it bleaches it. This is the opposite effect to that seen with madder or alizarin, which combines with calcium, as shown by Macklin,²⁴ and is deposited with it as a colored compound if the dye is present at the time of deposition.

22. Harting: On the Artificial Production of Some of the Principal Organic Calcareous Formations, *Quart. J. Micr. Sc.* 12:118, 1872.

23. Blotevogel, Wilhelm: Beiträge zur Kenntnis der Stoffwanderungen bei wachsenden Organismen: II. Der vitale Farbstofftransport während der Zahnentwicklung, *Ztschr. f. Zellen-u. Gewebelehre* 1:601, 1924.

24. Macklin, C. C.: Studies in Calcification by the Use of Vital Dyes, *J. M. Research* 31:493, 1917.

PLATE IV

Fig. 10.—Photomicrograph of a section through a cuboid slightly further advanced than that shown in figures 4 and 7. The cartilage cells are in irregular groups with darkly staining heavy trabeculae between them, which will become calcified and form the scaffolding for the future deposit of bone; $\times 150$.

Fig. 11.—Photomicrograph with high magnification of the area in a cuboid which is just beginning to calcify. The cells lie closely packed in irregular groups and in the matrix between them can be seen the black, densely stained masses of calcium deposit which in favorable places, when not too heavy, can be seen to be composed of closely packed granules. In those lacunae which are sharply in focus the actual lacunar wall is seen to be free from granules; $\times 500$.

Blotevogel found conditions in bone similar to those in dentine, uncalcified matrix colored with trypan blue and calcified areas unstained. The osteoblasts, forming matrix on all sides of them, stored the blue evenly in contrast to the odontoblasts which, forming dentine only on one side, stored all the blue at that side. A definite direction of transport of material and an evident cellular activity in handling this material has been beautifully demonstrated here. It may be inferred that what can be done in the case of trypan blue could be done also in the transport of calcium salts. A definite cellular activity can be demonstrated in the formation of the organic matrix of tooth, bone and cartilage, and the evidence all seems to point to the occurrence of a similar process in the impregnation of this matrix with the calcium salts.

Further collateral evidences that cellular activity is responsible for the handling of calcium in bone and cartilage may be cited. In Vincent's²⁵ book on "Internal Secretions and the Ductless Glands" are many instances, given with reference to original papers, of the influence of hormones on the growth of bone. The changes in acromegaly, the increased stature in eunuchs, the increased growth of bone in cretins treated with thyroid extract and other instances all go to show the effects of hormones.

Hammet²⁶ showed that thyroid and parathyroid deficiencies produce marked changes in the bones, especially in proportions of water, organic matter and bone salts. Parathyroidectomy lowers the calcium and phosphorus content and increases the amount of magnesium. This author also showed that all bones are not equally sensitive to disturbances in hormone control, the humerus, for example, being less resistant than the femur.

Rachitic changes in the bones of rabbits and rats the thyroid glands of which were removed three weeks after birth were demonstrated by Kunde and Williams²⁷ in spite of the administration of adequate diets to the animals.

Fahr²⁸ described marked changes of the endocrine system in the case of osteogenesis imperfecta and expressed the belief that these

25. Vincent, S.: *Internal Secretions and the Ductless Glands*, Toronto, The McMillan Company, 1912.

26. Hammet, F. S.: *Studies of the Thyroid Apparatus: XLII. The Rôle of the Thyroid and Parathyroid Glands in the Growth of the Long Bones*, *J. Exper. Zool.* **47**:95, 1927; *XLIII. The Rôle of the Thyroid and Parathyroid Glands in the Growth of the Long Bones*, *ibid.* **47**:95, 1927; *XLIV. The Rôle of the Thyroid and Parathyroid Glands in the Chemical Differentiation of Bone During Growth* (Ash, Organic Matter and Water), *J. Biol. Chem.* **72**:505, 1927.

27. Kunde, M. M., and Williams, L.: *Studies on Experimental Cretinism: II. Nutritional Disturbances of Bones*, *Proc. Soc. Exper. & Med.* **23**:814, 1926.

28. Fahr, T.: *Endocrine System in Osteogenesis Imperfecta*, *Virchows Arch. f. path. Anat.* **261**:732, 1926 (*Child Devel. Abstr.*).

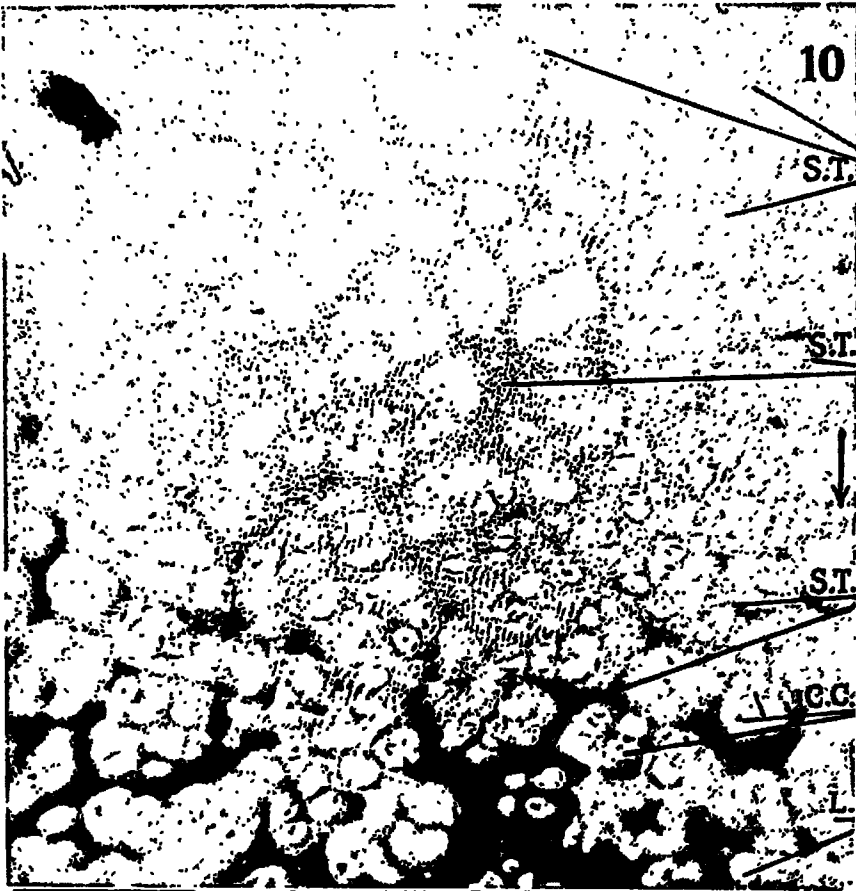


PLATE IV

changes are the fundamental factor causing dysfunction of the osteoblasts. By means of x-ray examinations on the living, Engelbach and McMahon²⁹ also showed marked changes in bone in various endocrine disorders. It is the general belief that hormones act on the cells of a tissue, which is much more probable, especially in the case of bone, than any hypothesis as to a chemical action on the matrix and its calcium content.

In a similar way vitamins are supposed to act on the cell, and McCarrison³⁰ showed marked changes in bone in cases of vitamin deficiency. In addition, Miles and Feng³¹ studied many cases of osteomalacia in China and came to the conclusion that it is a deficiency disease due to lack of fat-soluble vitamins. They noted that there might be a calcium deficiency in the diet and in the blood at the same time, but this was not always so. Without a deficiency of calcium in the body, such a condition as osteomalacia can be conceived of only as a disease in which the bone cell is at fault. It was also noted that administration of cod liver oil caused bone growth for more than two months after the cessation of treatment.

The normal growth of bone and the deposition of a proper calcium content in its matrix is stimulated by sunlight and by ultraviolet light in cases of rickets. This surely must occur by action on the tissue cells of the bone. In a review of the causes of rickets, Tisdall³² pointed out that a deficiency in the calcium content of the body is not sufficient in itself to cause this disease, whether the calcium is deficient either from diminished intake or from increased loss. A deficiency of vitamins alone or of phosphates alone will not produce rickets, but this deficiency leads only to osteoporosis by a failure to produce as large and heavy an amount of bone as necessary. Either a deficiency of calcium or a deficiency of phosphates combined with a deficiency in vitamins does, however, produce typical rickets. Robison and Soames³³ obtained similar results in experiments on rats. As every change in the various conditions already cited, except the deposition of the calcium in the bony matrix, is admittedly due to the activity of the bone cells, it seems reasonable to suppose that the deposition of calcium might also be ascribed to the cell's activities, as it occurs in such close correlation with

29. Engelbach, William; and McMahon, A.: *Osseous Development in Endocrine Disorders*, *Endocrinology* 8:109 (Jan.) 1924.

30. McCarrison, R.: *Studies in Deficiency Disease*, London, Henry Frowde and Hodder and Stoughton, 1921.

31. Miles, L. M., and Feng, C.: *Calcium and Phosphorus Metabolism in Osteomalacia*, *J. Exper. Med.* 41:137, 1925.

32. Tisdall, F. F.: *The Etiology of Rickets*, *Canad. M. A. J.* 11:934 (Dec.) 1921.

33. Robison and Soames (footnote 15, fifth reference).

It may be presumed that all the cartilage cells can excrete soluble phosphates and carbonates, yet calcium deposits do not surround all cells, but only those of one definite, particular zone.

If the cartilage cell secretes the calcium into the matrix, how does it accomplish it? Granules of the salts are not visible in the cell or its lacuna or passing through the capsule. The lacunae in cartilage are closed spaces, not a series of intercommunicating passages or canals through the cartilage, so one cannot look on them as open pathways conducting calcium salts in solution which might diffuse into the matrix and precipitate.

There are no blood vessels or lymph channels leading to individual cell lacunae in cartilage, and the common idea is that cartilage cells obtain all needed nutrient by imbibition of dissolved substances which diffuse through the matrix.

If, therefore, the cell obtains a supply of calcium it does so in dissolved form by diffusion through the same matrix in which the deposition is later made in solid form. This disposes of any view that the salts are excreted in liquid form and then precipitated in the matrix by lowering of carbon dioxide content, for the same matrix would have to possess a constitution which would allow calcium to pass in solution into the cells but not out again without being precipitated; this appears absurd. That there is calcium in the cartilage cells has also been demonstrated by Rabl.²

In studying the precipitation of calcium phosphate and carbonate in colloids in vitro, I noted a significant fact. With similar concentrations of reagents, it was more difficult to produce precipitation of the calcium salts in aqueous extracts of cartilage than in any other medium employed. There was always a much smaller quantity of precipitate obtained in these cases. This forms a strong argument against the view that cartilage calcifies by a simple precipitation reaction. Bechhold³ also noted that cartilage shows a selective adsorption of calcium.

From experiments on puppies, Jones⁴ concluded that two factors influence calcification. The more important one is the metabolic state inherent in the animal, and the other is diet, which influences the metabolism of the cells. The balance of ions between the bone-forming cells and their surroundings determines the deposition of bone salts. Any agent changing the metabolism of the bone cells will alter this ionic balance and will influence the deposition or the absorption of bone.

2. Rabl, R. H.: Ueber die Kalkablagerung bei der Knochenentwicklung, *Klin. Wchnschr.* 2:1644, 1923.

3. Bechhold, H.: *Colloids in Biology and Medicine*, translated by J. G. M. Bullowa, New York, D. Van Nostrand Co., 1919.

4. Jones, Martha R.: Studies on Inorganic Salt Metabolism: III. On Certain Factors Which Influence the Deposition and Resorption of Bone, *Am. J. Physiol.* 79:694, 1926-1927.

all the other activities. Medes³⁴ showed that the bones of rats on a diet poor in phosphorus exhibit rachitic changes, while diets low in calcium content lead only to osteoporosis.

It is to be particularly noted that cells having to do with the special use of calcium for structural purposes are not all of one kind. Three types of epithelium are found capable of secreting calcium to form solid structures: namely, the epithelium of the mantle of the clam, the epithelium of the shell gland of the bird, and that of the enamel organ of the tooth. Three types of connective tissue cells are similarly concerned: the cartilage cell, the osteoblasts and bone corpuscles and, finally, the odontoblasts of the teeth.

The view is readily accepted that the shell of the clam and the shell of the bird's egg are products of secretion, both the organic matrix and the calcium salts being present through the secretory function of the cells. It is generally admitted also that the organic matrix of bone and cartilage and of the enamel and dentine of the tooth are products of the cell. In the latter cases, why should not calcium also be present because of the secretory activity of the cells?

SUMMARY

Development of Bone.—1. Intramembranous bone develops by the simple calcification of a fibrous matrix, osteoblasts gradually walling themselves in with a finely granular deposit.

2. The formation of endochondral bone shows a progressive series of marked changes. The cells in the cartilage that are about to change enlarge, and the matrix increases in quantity and stains poorly. The cartilage cells then become segregated into groups between which lie the main, heavy trabeculae, and the matrix again stains deeply and calcifies by deposition of granules.

Blood vessels bearing osteoblasts now invade the calcified cartilage, eroding the narrower trabeculae and occupying the lacunae, from which the cartilage cells have disappeared. Osteoblasts deposit true bone on the remaining trabeculae; this first bone and the calcified trabeculae on which it lies are later reorganized, and an arrangement better suited to the structure as a whole is laid down.

A calcified cartilage skeleton, temporary in duration and replaced by bone, is an evolutionary phenomenon and repeats in the individual the history of the race.

Endochondral bones of different shapes and sizes show individual modifications in their process of development.

34. Medes, G.: Rats on Diets High in Phosphorus and Low in Calcium, *Proc. Soc. Exper. Biol. & Med.* 23:679, 1926.

A definite proportion was shown by Wells⁵ to exist between the amount of calcium carbonate and phosphate in bone and calcified cartilage. In normal persons, there are fifteen parts of calcium carbonate to eighty-five parts of calcium phosphate, or in the chemical proportions of one molecule of the carbonate to three of the phosphate.

The salts present in bone have been recently analyzed by Howland, Marriott and Kramer.⁶ They concluded that calcium is present only in the form of neutral calcium carbonate and tricalcium phosphate. The ratio of phosphate to carbonate depends directly on the amount of phosphates in the blood serum and is therefore lower in rickets, in which the phosphorus content is markedly reduced, than it is in health. In artificial mediums the ratio of phosphate to carbonate in the precipitate is in direct proportion to the quantities dissolved in the mediums, and can be obtained in the same relative amounts as in bone. However, the authors stated that the latter fact must not be taken to indicate that calcification is a process of simple precipitation, as they have shown that other factors have to be taken into account.

Shipley, Kramer and Howland⁷ took slices of cartilage from developing bones and immersed them in solutions containing calcium salts, where they were then incubated. Calcification of the cartilage occurred in nine hours with normal blood concentrations of calcium and phosphorus and at the normal hydrogen ion concentration of serum. This calcification was always in the matrix, never in the cells, and was not on the surface of a slice, but always in the depths of its thickness. Microscopic examination did not show any differences from the calcification of cartilage seen during normal development of bone.

Costochondral junctions in children dying of rickets did not calcify in rachitic serum, but the process did occur when they were immersed in normal serum.

Calcification did not occur after the cartilage was boiled or after the use of antiseptics or protoplasmic poisons. This clearly indicates the active part which the cell must play in the process.

With the addition of 1 per cent of egg albumin to the solutions, calcification did not occur in forty-eight hours, but if the slices of cartilage were washed at the end of twenty-eight hours and placed in fresh solutions without albumin calcification took place. This indicates that calcium when bound to a protein is not easily utilized by the cell,

5. Wells, H. G.: *Pathological Calcification*, J. M. Research 9:491, 1906; *Calcification and Ossification*, Harvey Lectures, 1910-1911; *Calcification and Ossification*, Arch. Int. Med. 7:721 (June) 1911; *Chemical Pathology*, ed 3, Philadelphia, W. B. Saunders Company, 1918.

6. Howland, John W.; Marriott, McKim and Kramer, B.: *Studies Upon the Inorganic Composition of Bone*, J. Biol. Chem. 68:721, 1926.

7. Shipley, P. G.; Kramer, B., and Howland, J.: *Studies upon Calcification in Vitro*, Biochem. J. 20:379, 1926.

(a) Long bones are invaded at the center of the shaft by blood vessels which bud and grow rapidly and carry in osteoblasts with them. Calcified cartilage always lies just ahead of the vessels and is continually invaded and its line pushed back until the whole shaft is ossified. The calcified cartilage grows away from the entering vessels. Blood vessels are not present in the shaft before the process of ossification begins.

(b) Epiphyses and short irregular bones such as the carpals and tarsals contain blood vessels long before ossification begins. These vessels extend about half way to the center and then branch and anastomose. The central area bounded by them calcifies and is then invaded by budding vessels carrying in osteoblasts. The cartilage is eroded except for some larger trabeculae; the zone is ossified and then extends its boundaries until it reaches the periphery of the bone. In this case the calcified cartilage extends toward the entering blood vessels, not away from them as seen in the shafts of long bones.

(c) Endochondral bones of the skull may show enlargement of the cartilage cells and calcification of the matrix without the presence of any blood vessels until the moment when they are penetrated by budding vessels accompanied by osteoblasts.

Form of Calcium Deposits.—1. In Cartilage: The deposit is always in the form of distinct granules which accumulate in closely packed masses but do not fuse. The granules appear first in the matrix immediately around the cartilage cells, but there appears to be a thin envelop or capsule forming the actual wall of each lacuna which is free from granules. The granules appear first around those cells nearest to blood vessels.

2. In Bone: The deposit is always granular. The granules are minute, much smaller than those in cartilage, and they may fuse to form a homogeneous mass. The granules appear first in the matrix in immediate contact with the osteoblasts.

Manner of Deposition of Calcium Salts.—In normal calcification of cartilage and bone, the deposition of the calcium salts is presumed to be due to cellular activity, because the first evidence of deposition is always immediately about the cell and can occur only after definite changes in the cell and in the organic matrix formed by it (Watt). It has also been shown that precipitation of calcium salts is difficult in a cartilage extract (Watt¹⁸), and solutions of calcium phosphate in conditions similar to those in the tissues can exist for a long period without precipitating (Holt, LaMer and Chown¹⁹) and normal blood is 200 per cent saturated.

Slices of normal living cartilage will calcify rapidly when incubated in proper solutions, but will not do so if the cells are killed (Shipley, Kramer and Howland⁷). Cells forming the enamel and dentine of the

and that it is the ionized calcium in the blood serum which is readily available for calcification.

That part of the calcium in the blood serum is not ionized and is bound to some protein was demonstrated by Marrack and Thacker,⁸ who also showed that a change of hydrogen ion concentration of from 7.4 to 7.8 reduces the calcium ion concentration 60 per cent. In regard to the latter point the work of Jones is significant, as she showed that destruction of bone in rickets is much greater as the alkalinity of the tissues is increased by appropriate diets and healing tends to occur with the administration of acids.

A nondiffusible, nonionizable portion of the calcium in the blood, bound to a protein component, was also shown by Updegraff, Greenberg and Clark,⁹ and by Hastings, Murray and Sendroy.¹⁰

Freudenberg and György¹¹ expressed the belief that in some way calcium is bound to the protein constituent of the cartilaginous matrix and reacts with phosphates and carbonates to form the hard deposit evident in calcification. Products of tissue degeneration as well as urea and ammonium salts prevent calcification. The phosphate and carbonate formed may secondarily split off as inorganic salts from the protein and leave the latter free to repeat the process, thus increasing the calcification.

According to Bergeim, rachitic rats lose both calcium and phosphorus in the feces, while normal animals absorb these elements. Therefore, rickets is not only a pathologic condition of the bone but shows derangement of other parts of the body. Telfer¹² demonstrated similar conditions in human beings and showed that administration of cod liver oil caused great increase in absorption of both calcium and phosphorus.

8. Marrack, J., and Thacker, G.: *The State of Calcium in Body Fluids*, *Biochem. J.* 20:580, 1926.

9. Updegraff, H.; Greenberg, D. M., and Clark, G. W.: *A Study of the Distribution of the Diffusible and Nondiffusible Calcium in the Blood Sera of Normal Animals*, *J. Biol. Chem.* 71:87, 1926.

10. Hastings, A. B.; Murray, C. D., and Sendroy, J., Jr.: *Studies of the Solubility of Calcium Salts: I. The Solubility of Calcium Carbonate in Salt Solutions and Biological Fluids*, *J. Biol. Chem.* 71:723, 1926. Sendroy, J., Jr., and Hastings, A. B.: *II. Solubility of Tertiary Calcium Phosphate in Salt Solutions and Biological Fluids. III. Solubility of Calcium Carbonate and Tertiary Calcium Phosphate Under Various Conditions*, *J. Biol. Chem.* 7:783, 1926.

11. Freudenberg, E., and György, P.: *Kalkbindung durch tierische Gewebe*, I to X *Biochem. Ztschr.* 110:299, 1920; 115:96, 1921; 118:50, 1921; 121:131, 1921; 121:142, 1921; 124:299, 1921; 129:134, 1922; 129:138, 1922; 142:407, 1923; 147:191, 1924.

12. Telfer, S. V.: *Studies in Calcium and Phosphorus Metabolism: IV. The Influence of Free Fatty Acids in the Intestine on the Absorption and Excretion of the Mineral Elements. V. Infantile Rickets. The Excretion and Absorption of the Mineral Elements and the Influence of Fat in the Diet on Mineral Metabolism*, *Quart. J. Med.* 20:1, 1926.

teeth show a definite storage and direction of transport of trypan blue and bone cells show similar activities (Blotevogel²³).

Secretions of the ductless glands exert a marked influence on growth of bone, and cell tonics such as sunlight, ultraviolet light and vitamin also show marked effects. Bone and calcifying cartilage are shown to possess a ferment, esterase, which will convert organic phosphates into inorganic compounds (Kay and Robison¹⁶).

Collateral evidence of the power of cells to secrete calcium salts to form hard structures is shown by the epithelium of the mantle of the clam in producing the clam shell and the epithelium of the shell gland in producing the shell of the bird's egg.

Bones become rarefied when blood calcium is low, as in pregnancy and in increased loss from the body in certain fistulas. There seems to be a calcium balance between blood, bone cell and bone matrix something like the sugar balance in the liver.

All the foregoing points seem to point toward cellular activity in the calcification of bone and cartilage. Thus, six types of cells can secrete calcium to form hard structures: three epithelial cells—the ameloblast which builds enamel of the teeth, the epithelium of the mantle of the clam, and the epithelium of the bird's shell gland—and three types of connective tissue cell—the odontoblast which builds dentine in the teeth, the cartilage cell, and finally the osteoblast and bone corpuscle.

In the later stages it was found that the stump again assumed its normal color and had areas which showed crepitation, but the site that was exposed was found firmly adherent to the nearest portion of the wall of the chest. The strands of compression near the suture and also flattening of the bronchioles were seen microscopically. Some bronchioles lost their major characteristics and could be recognized only by the cartilage or the remnants of bronchial epithelium. In some areas an entire loss of alveolation was found, and the whole field contained dense fibrous tissue. In the crepitating areas, the characteristic alveolation but also a characteristic increase in the interstitial fibrous tissue



Fig. 3.—Section from the stump eighty-one days after lobectomy. The strand formation of the alveoli caused by the silk suture should be noted.

with proportional decrease in the size of the alveolar spaces have been found.

In the presence of infection, changes characteristic of pneumonia were noticed as well as areas in which there was a localized deposition of polymorphonuclears but no destruction of the center. In such cases, lobar pneumonia in the contiguous lobe and even on the opposite side was also noticed.

In all cases, a thickening of the pleura around the stump was found. This thickened pleura and the adhesions are the best allies in giving good results.

The contiguous lobe or the lung on the opposite side may show any of several changes. It may remain normal; it may show lobar pneumonia, edema, and, most frequently, an interstitial thickening.

Secondary operations on the same or opposite side have not been borne well by these dogs. It is possible that the anesthetic has something to do with it. Ether has been used throughout. One animal, which was thought to have recovered completely, was operated on 101 days after the first operation. This dog died on the table in the middle of the operation. It did not take the anesthetic well in spite of the satisfactory anesthesia and artificial respiration.

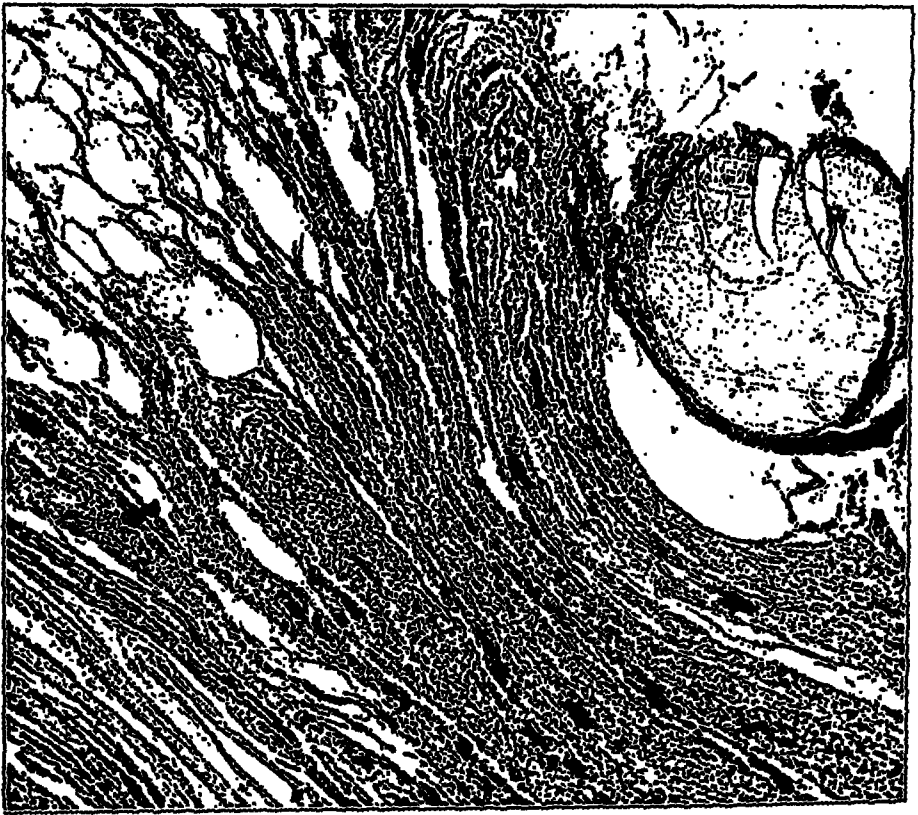


Fig. 4.—Section from the stump 101 days after lobectomy. The strand formation of the alveoli at the point of compression and the gradual return to normal alveolation beyond the catgut suture should be noted.

COMMENT

The results in these experiments were encouraging. In only one case were infection and leakage of air at the stump encountered. In all the others, the stump remained airtight and watertight. It was noticed that when the dogs were left alone after the operation they might live indefinitely, if they survived the first six days. It is possible that the removal of a lobe or the whole lung will cause a definite strain on the circulation, with a subsequent acute or subacute edema which eventually causes asphyxia in the dog. Moreover, if the wall of the chest is left

OXYGEN IN THE TREATMENT OF POSTOPERATIVE BRONCHOPNEUMONIA *

MELVIN W. BINGER, M.D.

Fellow in Medicine, The Mayo Foundation

E. STARR JUDD, M.D.

ALEXANDER B. MOORE, M.D.

AND

RUSSELL M. WILDER, M.D.

ROCHESTER, MINN.

In the symposium on treatment with oxygen in cases of pneumonia that was presented last year at the meeting of the Association of American Physicians, Binger,¹ Barach² and Boothby³ suggested that the disrepute of such treatment could be accounted for by the ineffectiveness of former methods of administering the oxygen. They then described the newer apparatus, the oxygen chamber and the oxygen tent, by means of which it is possible to envelop the patient, or his head, in an atmosphere of any concentration of oxygen desired. They demonstrated that with atmospheres of about 50 per cent oxygen, anoxemia could usually be controlled, and the patient with pneumonia improved subjectively; the temperature and pulse often fell dramatically.

The present report is concerned chiefly with the treatment with oxygen in cases of postoperative pneumonia at The Mayo Clinic. Up to Jan. 1, 1927, oxygen had been used in only a few cases, but by this time a fleet of tents had been put into service, and approximately 50 per cent of the patients in whom pneumonia developed in 1927 were treated with oxygen. Therefore, if such a procedure has definite merit, it should be reflected in the mortality statistics of this year. The following data were noted:

In 1927, the pathologist named pneumonia as the cause of death in thirty-six of the postoperative cases which came to necropsy. During the preceding four years, there had been an average of forty-eight deaths, with a fluctuation, however, of from thirty-nine to fifty-six.

* Read before the Association of American Physicians, Washington, D. C., May 1, 1928.

* From The Mayo Clinic, Rochester, Minn.

1. Binger, C. A. L.: General Considerations in Regard to Oxygen Therapy, Tr. A. Am. Phys. 42:301, 1927.

2. Barach, A. L.: Acute Disturbance of Lung Function in Pneumonia, Tr. A. Am. Phys. 42:303, 1927.

3. Boothby, W. M., and Haines, S. F.: Oxygen Therapy, Tr. A. Am. Phys. 42:287, 1927.

Malacoplakia.—Berg⁵¹ reported a case of malacoplakia of the bladder which had been under treatment since 1907, at which time the patient had passed two stones 0.3 cm. in diameter. The diagnosis was made by cystoscopic examination. The patient returned eighteen years later with calculous pyonephrosis on the right side. Nephrectomy was followed by uneventful convalescence. Cystoscopy three months later revealed the same picture in the bladder as had been noted eighteen years previously, except that the areas were slightly smaller and better defined. Berg believed that the process resulted from irritation due to the stones. The plaques themselves did not cause symptoms.

[ED. NOTE.—Several reports on malacoplakia of the bladder have appeared recently. Certain writers have suggested that they are a precancerous condition, others that they cause many vague symptoms. This report of Berg is interesting in that it suggests that malacoplakia may be an entirely innocuous condition.]

Grieg⁵² reported a case of a multipara, aged 30, with a suprapubic tumor which had grown large over a period of eight months. It was smooth, oval and painless, was not freely movable, and did not fluctuate. It lay between the umbilicus and symphysis. Pain in the loin, radiating to the thigh was present. With the assumption that a uterine or ovarian tumor was present, laparotomy was undertaken. The tumor was extra-peritoneal and easily isolated. There was no connection with the umbilicus, although there was a connection between its lower pole and the bladder. The patient was living and well seven years after removal of the tumor. Microscopically, the tumor was found to be a spindle cell sarcoma.

Twenty malignant tumors of the urachus were also noted; eight deaths followed surgical removal. Twelve of the twenty tumors were carcinomas and eight were sarcomas.

Contracture of the Neck of the Bladder.—Knorr⁵³ reported two cases of sclerosis and four of contracture of the neck of the bladder in women. The former ran a chronic course, resulting finally in repeated attacks of urinary retention. In both of these cases there had been a previous inflammatory condition of the neck and the trigone of the bladder, in one case due to staphylococcus and in the other to the colon bacillus. In the cases of contracture, which is a condition of muscular cramp, cystitis of the neck and trigone was also an etiologic factor.

51. Berg, G.: Zur Malakoplakia vesicae, Verhandl. d. deutsch. gesellsch. f. urol., 1927, p. 306.

52. Grieg, D. M.: Report of a Case of Sarcoma of the Urachus, Edinburgh Med. J. 34:425, 1927.

53. Knorr, R.: Ueber Kontraktur und Sklerose des Blasenhalsses beim Weibe, Zentralbl. f. Gynäk. 51:1154, 1927.

In 1927, sixteen deaths were attributed to pneumonia in cases in which operation had been performed on the stomach or duodenum. Usually the diagnosis was made at necropsy by the pathologist; sometimes it was made by the surgeon. In the preceding year (1926), when little oxygen was used, the number of deaths from pneumonia in the corresponding group of cases was twenty-two. The deaths from all causes following operation on the stomach and duodenum fell from sixty-two in 1926, to fifty-three in 1927, a reduction of the mortality rate of 20 per cent, chiefly attributable to fewer deaths from pneumonia (table 1).

In the hospital in which most operations of the upper part of the abdomen were performed, the deaths from pneumonia diagnosed at necropsy in 1927 were twelve (in 8,124 operations) as opposed to

TABLE 1.—*Operations on the Stomach and Duodenum*

| Year | Operations (Cases) | Deaths, All Causes | | Deaths from Pneumonia | |
|-----------|-----------------------|--------------------|----------|-----------------------|------------------------|
| | | Cases | Per Cent | Cases | Per Cent of All Deaths |
| 1926..... | 1,303 | 62 | 4.45 | 22 | 36 |
| 1927..... | 1,482 | 53 | 3.57 | 10 | 30 |

TABLE 2.—*Comparative Mortality in Two Hundred and Five Cases*

| Treatment Started, Days After Operation | Cases | Deaths, All Causes | | Deaths, Pneumonia Cases |
|---|-------|--------------------|----------|-------------------------------|
| | | Cases | Per Cent | |
| 1 to 4..... | 159 | 19 | 12 | 4 |
| 5 or more..... | 47 | 35 | 74 | 18 |

twenty-two (in 7,866 operations) in 1926. Oxygen had not been used in three of the twelve cases in 1927, and it had been resorted to tardily in six cases. Only three of these deaths can be attributed to failure of treatment with oxygen.

We observed 205 cases of postoperative pneumonia in which the patients were treated with oxygen. The diagnosis was confirmed in most instances by roentgenograms. If this series of cases is divided arbitrarily into those in which treatment with oxygen was started before the fifth day after operation, and those in which it was started after the fourth day, it is shown that the mortality in the latter group is six times as high as that in the former group: 74 per cent as opposed to 12 per cent (table 2). The fourth day after operation is late in many cases, since evidence of the onset of pulmonary complications can usually be detected within the first twenty-four hours after operation and the condition of the patients may be serious much earlier than the fourth day.

Slow and cautious dilatation of the sphincter is the suitable treatment in most cases.

Frühwald⁵⁴ found in a series of 1,300 endoscopies 372 cases of lesions at the neck of the bladder due to infection. Most of the patients were women. Specific urethritis was present in 42 per cent of the cases. The type of changes are: (1) in from four to six weeks following infection small nodules with circumscribed edema can be seen; these may disappear spontaneously; (2) in three months small filiform and transparent efflorescences appear, and (3) in four months polyps of various sizes, shape and form (finger-like, club-like, cock's comb-like, forked, and cauliflower-like) appear. These polyps are occasionally the underlying cause of resistant gonorrhea; they are found even though the gonococcus is not present, and they may be the cause of persistent infection after apparent cure. These changes could only be found in 4 of 171 control cases in which there had never been any sign of gonorrheal infection. Etiologically, gonorrhea plays the chief, but not the only part. Histologic examination shows that possibly these polyps are developed from preformed epithelial nests which multiply by irritation, usually the result of gonorrhea.

Lesions of the Nerves.—McCrea⁵⁵ concluded that the vesical symptoms of tabes are of two chief clinical types: the incontinent, in which there is a definite cutting off of sensation from the higher centers, and the parietic, in which the sensory loss, although present, is not so apparent, being concealed by the interference with reflex function of the viscus. A third type exists in which the symptoms are mixed, but this type is rare. In the parietic bladder, the more prominent symptoms are due to interference with the reflex function of the organ, and are largely the result of lesions of the afferent fibers running in the autonomic pelvic nerves. In the incontinent bladder, the most obvious symptoms are similar to those of a lesion of the sensory pathway in the cord, and this sensory loss is significant in the production of muscle senses which are transmitted by the pudic nerves.

McCrea suggested that tabes may rarely affect the autonomic or visceral nerves and the somatic sensory nerves simultaneously, and if it does, never to the same degree. This explains the difference between the pelvis and pudic nerves. The most obvious cases of tabes are those presenting destruction of somatic sensory fibers, but not visceral crises.

54. Frühwald: Veränderungen am Orificium internum urethrae bei Gonorrhoe der Frau, *Dermat. Wchnschr.* 84:376, 1927.

55. McCrea, E. D.: Bladder in Tabes, *Irish J. M. Sc.*, 1927, p. 658.

It is recognized that these data do not constitute biometric proof of the efficiency of treatment with oxygen. Nevertheless, in view of the fact that the treatment was given in not more than 50 per cent of all cases of postoperative pulmonary complications, that in many of these the oxygen was administered late, and that there were no other significant innovations in the treatment of patients before or after operation in 1927, we feel justified in concluding that lives have been saved.

In an endeavor to obtain other evidence of the value of the procedure, we resorted to experiments on animals. Smith⁴ recently reported that he had caused aspiration pneumonia in guinea-pigs and rabbits by the intratracheal injection of infected material. Dogs are resistant to such procedures, as Cutler and Schlueter⁵ have noted, but the guinea-pig proves to be surprisingly sensitive. By anesthetization with ether, exposure of the trachea by operation and intratracheal injections, we produced pneumonia almost constantly with streptococci freshly cultured from healthy throats. Furthermore, the pneumonia almost always proved fatal, most of the animals dying from extensive bronchopneumonia within two weeks. A series of such experiments was conducted. In each experiment, ten or twelve guinea-pigs were anesthetized and inoculated in an identical manner, and then half of them were subjected immediately after the operation to an atmosphere of 50 per cent oxygen and left in this atmosphere for twenty-four or forty-eight hours. The results encourage us to believe that oxygen properly administered is a life-saving measure. Sixty-six of seventy untreated guinea-pigs died within two weeks. Six of fifty-one treated guinea-pigs were killed from the second to the sixth day for examination of the lungs; twenty-two guinea-pigs died and twenty-three survived. The mortality of the treated guinea-pigs is, thus, at least 50 per cent less than that of the untreated guinea-pigs.

During the last four months, in selected cases on one of the surgical services, treatment with oxygen has been started immediately after operation and continued for from twenty-four to forty-eight hours. The patients chosen were those who had had recent colds, who were elderly or feeble, or who had been operated on in the upper part of the abdomen; in other words, they were patients concerning whom there was reason for apprehension in a consideration of postoperative pulmonary complications. Although this group was small, it is encouraging that pulmonary infection did not develop in a single instance.

4. Smith, D. T.: *Experimental Aspiratory Abscess*, Arch. Surg. 14:231 (Jan.) 1927.

5. Cutler, E. C., and Schlueter, S. A.: *The Experimental Production of Abscess of the Lung*, Ann. Surg. 84:256, 1926.

Fistula.—Roeder⁵⁶ pointed out that the interference with the blood supply of the lower part of the ureter and bladder following total hysterectomy, as a cause of postoperative ureteral and vesical fistula, deserves more consideration than it has received in the past.

The blood supply of the inner portion of the anterior vaginal wall and the apposed bladder comes from branches which originate from the inferior vesical and uterine arteries. The uterine arteries send branches to surround the vault of the vagina, the anterior branches uniting to form a single vessel which runs forward in the median line of the anterior vaginal wall. This is the *arteria azygos vaginae*. Large fistulas may result from blocking of these vessels in the performance of total hysterectomy.

In two patients treated by Roeder, so much bladder tissue was destroyed that it would have been impossible to approximate the edges even after extensive dissection. Roeder, therefore, made an incision in the vaginal walls through their entire thickness, starting 2.5 cm. or more from the fistula. Thick flaps were turned back to afford an ample supply of blood. These flaps of vaginal wall were dissected up to within 0.8 cm. of the margin of the fistula. The flaps were then united by several layers of chromic catgut sutures, the first suture being pulled through the wound of a previously performed suprapubic cystostomy and kept under slight tension to assist in coaptation of the vaginal flaps. The bladder was left open for drainage and a self-retaining catheter placed in the urethra. In the area remaining after the vaginal flaps had been turned into the bladder, a drainage tube was placed and brought to the surface paravaginally. This was done to prevent possible leakage of urine through the vagina and the reestablishment of the fistula.

The postoperative care involved irrigation of the urethral catheter twice daily; the irrigation was allowed to come through the suprapubic tube or wound. The drain inserted paravaginally was left in for about ten days. Results from the operation were satisfactory in both of Roeder's cases, although one of the patients died twelve days afterward from chronic nephritis and hepatitis. Necropsy showed that the bladder was firmly united at the site of repair.

Young⁵⁷ stated that the vaginal approach in operating on vesico-vaginal fistulas is not always satisfactory. He reported the case of a woman, aged 31, whose bladder was accidentally opened during the removal of a hydatid mole. Eleven operations over a period of three

56. Roeder, C. A.: A Technique for the Repair of Large Vesicovaginal Fistulae, *Surg. Gynec. Obst.* 45:102, 1927.

57. Young, H. H.: Repair of Vesicovaginal Fistula: Presentation of New Instrument, *Surg. Gynec. Obst.* 45:226, 1927.

COMMENT

There is reason to believe that treatment with oxygen has resulted in the actual saving of life. The good results have occurred chiefly in the group of cases in which treatment was instituted reasonably early. Administration of oxygen immediately after operation and before the development of pulmonary lesion promises to be an effective method for preventing the occurrence of serious pulmonary complications.

years had been undertaken elsewhere in an attempt to close the fistula, but in each instance the wound had broken down and the fistula persisted. The patient's health was good and renal impairment was not demonstrable.

On examination, the uterus appeared to be normal. Slightly to the right of the median line on the anterior wall of the vagina was an area of induration with a slight depression in the center. On cystoscopy, about 20 cc. of clear urine was evacuated. The capacity of the bladder on forced distention was about 300 cc. The trigone was much distorted. Running forward and outward from the right side of the trigone was a peculiar band of tissue which was entirely separated from the wall of the bladder, except at its upper and lower ends; this bridge was entirely covered with mucous membrane. Beneath the band was the opening of the vesicovaginal fistula. The fistula could be seen from either the inner or the outer side of the bridge which spanned its orifice. The ureteral orifices could not be made out, but it was believed that the right orifice was near the fistula, and it did not seem wise to close the fistula by the vaginal route.

Suprapubic operation was carried out; the bladder was opened extraperitoneally in the median line and the orifice of the small vesicovaginal fistula was disclosed. The muscular bridge was excised. A small hook was made on the end of a large safety-pin. This was pushed through the fistula and then drawn outward. One side of the fistulous tract was impaled on the pin and drawn upward. The fistulous tract was then completely excised by a circular incision under vision. The large opening between the bladder and vagina was closed by means of purse string sutures placed through the bladder. The first layer was through the submucosa of the vagina and did not penetrate through the mucosa. This suture was of heavy chromic catgut and was tied through the bladder, thus securing complete closure of the vaginal opening. The next suture was of plain catgut treated with mercurochrome-220 soluble and approximated the musculature of the bladder; this left an irregular defect in the mucosa which was closed in a linear direction by means of a through-and-through plain catgut suture tied intraventrically. The insertion of these sutures, it is to be emphasized, was facilitated by the introduction of the index finger in the vagina to elevate the site of the fistula. The bladder was closed around a large Pezzer catheter.

During the earlier days of convalescence, the patient lay on the abdomen, face downward, as suggested by Chute. Young considered this an important detail. On the tenth day she was allowed to lie on her back, but the suprapubic catheter was kept in place for three

A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.

LOS ANGELES

E. STARR JUDD, M.D.

ROCHESTER, MINN.

LINWOOD D. KEYSER, M.D.

ROANOKE, VA.

GORDON S. FOULDS, M.D.

TORONTO

JEAN VERBRUGGE, M.D.

ANTWERP, BELGIUM

AND

ADOLPH A. KUTZMANN, M.D.

LOS ANGELES

(Concluded from page 898)

BLADDER

Tumors.—Beer,⁴³ at the Third Congress of the Society of International Urologists, stated that the employment of high frequency currents through the cystoscope has given excellent results in the treatment of tumors of the bladder. There are known differences in the action of the unipolar and bipolar current. The unipolar is more explosive and of a higher tension and requires greater amperage. The action of the bipolar current is more useful in producing extensive coagulation of the pedicle of a tumor. When the bladder is open, the papilloma may be held up with a clamp and the bipolar current allowed to penetrate through the tumor, which produces coagulation that extends through the pedicle in the adjacent wall of the bladder.

Beer has had excellent results in the endoscopic treatment of vesical tumors in 158 cases. In about 20 per cent of the cases, there were recurrences. Recurrences in the same site are usually due to insufficient destruction.

In the operative treatment of tumors of the bladder, Beer stated that it is necessary to prevent implantations of tumors. He suggested bringing the bladder outside the peritoneal cavity for a good exposure. The bladder should be opened with a radio knife and the various tumors coagulated and removed. Results with this treatment were satisfactory in thirty-three cases; 85 per cent of the patients were apparently cured. He has employed radium emanation planted through the cystoscope in sixteen cases with successful results in 50 per cent. The poorest results were obtained in cases of inoperable carcinoma situated in the

43. Beer, M. E.: *Traitement des tumeurs de la vessie, par les agents physiques*, J. d'urol. 24:327, 1927.

weeks. Complete recovery with healing of the fistula and good function of the bladder resulted.

Young described several instruments for thus impaling the fistulous tract and elevating it under the operator's view so that it may be carefully dissected out. A thin tractor with two spreading blades, similar to Young's prostatectomy tractor, but with delicate nonfenestrated blades, is suggested as a suitable instrument.

[ED. NOTE.—Vesicovaginal fistula is usually attacked from below through the vagina, possibly because of the success which first attended the operation of Sims. It is interesting to note that both Roeder and Young have recently reported operations by the transvesical route. Certainly the expedient appears favorable to those who have failed with this stubbornly recurrent condition. The surgical principles of removing the mucous membrane in such a way as to prevent its regrowth between the vagina and bladder is well established. Eversion of the mucosa of the vagina into the vagina away from the bladder and invasion of the mucosa of the bladder into the bladder away from the vagina in the process of closing the defect have been emphasized in contemporary literature. The transvesical approach, together with dependent drainage of the bladder during convalescence, seems theoretically to be satisfactory. The experience of Roeder and Young seems to show that their methods are practical.

Tuberculosis.—Ormond reported a case of severe tuberculosis of the bladder which failed to improve following right nephrectomy. The remaining kidney was almost totally without function. Inguinal ureterostomy relieved the patient greatly, and function in the remaining kidney was partially restored. Treatment consisted of local, general and medication for local effect. Numerous drugs have been recommended to be taken by mouth, such as methylene-blue, guaiacol in 5 mm. capsules, belladonna, hyoscyamus and oil of sandalwood. Heliotherapy, the use of tuberculin, general nutritional methods and drugs administered hypodermically are also recommended. Local treatment has varied greatly. Because irrigations are painful, instillations have been advocated. The following drugs have been used: mercuric chloride 1:5,000 to 1:1,000; iodoform in liquid petrolatum; 5 per cent guaiacol with iodoform in petrolatum; gomenol, from 10 to 20 per cent in oil; from 0.5 to 1 per cent picric acid; 5 per cent phenol; 1 per cent mercurochrome; 5 per cent silver nitrate; methylene-blue; iodine vapor and sterile air. Excision or fulguration of the ulcer is sometimes advised.

Four types of distressing intractable cases are cited in which further radical treatment is necessary: (1) bilateral renal tuberculosis;

region of the sphincter. In seventeen cases of carcinoma, deep roentgen-ray treatment was employed without any real cures. In certain cases, symptoms were ameliorated.

Löffler ⁴⁴ reported twenty-two cases of resection of the bladder performed at the Krankenhaus in Vienna. Twenty of the operations were performed for carcinoma; one was performed for sarcomatous carcinoma, and one for ulcer. Most of the resections were carried out through a longitudinal suprapubic cystotomy opening under lumbar anesthesia produced with 5 per cent tropacocaine. Ureters were reimplanted in cases of ureteral involvement. The immediate mortality was 27.3 per cent, and the late mortality 14.3 per cent.

Joseph ⁴⁵ stated that the intravesical treatment of malignant vesical tumors is only an emergency measure which has been frequently employed because surgical measures have been so hopeless. The so-called resection of tumors of the bladder, that is, removing part of the wall of the bladder, has in general given poor results. From a great number of cases in the literature, it has been noted that there were recurrences following operation in from 80 to 90 per cent. In many cases, the patient's life is probably shortened by resection and made worse by tenesmus, fistula formation and more rapid growth and spread of the tumor. The only exceptions are the cases in which the tumors are in the dome of the bladder, the upper aspect of the anterior wall or the upper part of the posterior aspect. Tumors in these situations are technically easier to resect. If, however, as is often the case, the tumor lies in the floor of the bladder, in the neck, or between the ureteral orifices, satisfactory resections are not technically possible. Destruction and total extirpation of the bladder cannot be considered for such cases; the patient with a small tumor will refuse this treatment for a continuance of the small amount of suffering, while the patient who has a large growth, even though consenting to the operation, has only a small chance of recovery.

The resection of a tumor of the bladder is nevertheless considered because of the occasional cure in the dome of the bladder. This is an incomplete attempt at cure and is comparable to a supravaginal amputation of the uterus in carcinoma of the body of the uterus or the enucleation of carcinoma of the breast without amputation or resection of lymphatics. Consequently, Joseph employs intravesical treatment of malignant tumors. This manner of treating vesical tumors has given,

44. Löffler, L.: *Unsere Fälle von Blasenresektion*, Verhandl. d. deutsche gesellsch. f. urol., 1927, p. 361.

45. Joseph, E.: *Die intravesicale Behandlung börsartiger Blasengeschwülste*, Verhandl. d. deutsche gesellsch. f. urol., 1927, pp. 323 and 364.

(2) tuberculosis of the remaining kidney, the other kidney having been removed for tuberculosis; (3) failure of the bladder to clear up following nephrectomy even though the remaining kidney is healthy, with the ureteral orifice becoming strictured and hydronephrosis resulting, and (4) advanced genital tuberculosis in the male. For treatment, the following methods have been brought forth: (1) complete excision of the bladder with implantation of the ureter into the intestine; (2) simple implantation of the ureter into the intestine; (3) implantation of the ureter to the skin of the groin, iliac or inguinal ureterostomy; (4) nephrostomy; (5) lumbar ureterostomy; (6) suprapubic cystotomy; (7) vaginal cystostomy, and (8) denervation of the bladder.]

Ormond⁵⁸ expressed the opinion that inguinal ureterostomy is the method of choice in most cases. It is easily performed, is short, relatively free from danger and the resulting fistula can be cared for satisfactorily.

Syphilis.—Gautier⁵⁹ reported a case of syphilis of the bladder. Several days after an injection of bismuth, frequency of urination and dysuria developed. On examination, a mass was felt above the prostate; this was situated in the median line and gave the same sensation as a vesical tumor. Cystoscopic examination revealed a large mass in the fundus of the bladder; its apex was an ulcerated crater. All signs and symptoms disappeared after extensive antisyphilitic treatment.

Gautier expressed the belief that the few preliminary injections of bismuth caused congestion of the bladder and attracted attention to that organ. He stated that cystoscopic examination should be performed in syphilitic patients who complain of any symptoms referred to the bladder.

Paralysis.—According to Boyd,⁶⁰ the dangers which come from overdistention of the bladder and their accompanying genito-urinary infections can be overcome in cases of acute paralysis of the bladder by suprapubic drainage. He stated that the objections to this procedure worth mentioning are few and that it has many advantages. The abdominal distention which so often exists and the lowered resistance of the tissues, due to paralysis of the abdominal wall, make certain precautions at operation necessary.

58. Ormond, J. K.: Diversion of the Urine in Intractable and Incurable Vesical Tuberculosis, *J. Urol.* 19:109, 1928.

59. Gautier, M.: Gomme syphilitique de la vessie, *Presse méd.* 2:55, 1928.

60. Boyd, M. L.: Suprapubic Cystotomy in Bladder Paralysis, *J. Urol.* 18: 413, 1927.

he believes, satisfactory results. Aseptic tumors with only a few symptoms are excluded. Two methods are considered: thermocoagulation and chemicocoagulation. Joseph uses a combination of both. He covers the bleeding tumors with concentrated trichloroacetic acid (chemico-coagulation), using a ureteral catheter through the cystoscope. This treatment is comparable to treatment of inoperable carcinomas of the uterus with zinc chloride. A large part of the tumor sloughs off with this treatment, the tumor becomes smaller and then becomes covered with normal mucous membrane; bleeding and oozing are practically checked. At the next treatment, the necrotic material due to the former treatment has sloughed off and trichloroacetic acid is used again. In order to make this treatment more efficient, the thermocoagulation is followed by another treatment of trichloroacetic acid, which gives the acid an opportunity to penetrate into the tumor.

It is understood that cure cannot be obtained from the chemico-coagulation or from the thermocoagulation and chemicocoagulation. Joseph has, however, achieved long enduring results in some cases, noting that many patients have good health and ability to work even with an inoperable tumor. He has not observed benefit from radium or deep roentgen-ray therapy and stated that in the United States the urologists are getting away from radiotherapy.

Privess⁴⁶ stated that adenomas of the bladder are not common. He reported a case in which the patient came for treatment because of hemorrhoids, but gave a history of urethral stricture, vesical distress and urinary retention. Urethral dilatation and cystoscopy revealed smooth vesical calculi and a tumor, 2.5 cm. in diameter, covered with normal mucous membrane near the neck of the bladder. Cystotomy was performed with the removal of fifty stones and extirpation of the tumor. Histologically, the tumor was similar to prostatic tissue and it was thought to be of prostatic origin. Adenomas of the bladder are benign, and become serious only by causing retention or hemorrhage. The stones were probably formed because of the obstruction to urination.

Gagucan⁴⁷ divided tumors of the bladder into four groups: (1) true papilloma, (2) papilloma with malignant degeneration, (3) carcinoma and (4) massive carcinoma.

The treatment by deep roentgen ray, while not always producing cure, sometimes causes amelioration of symptoms and regression of the size of the tumor. The combined results of radium and roentgen ray

46. Privess, M.: Ueber gutartige Geschwülste der Harnblase: Ein Fall von Cystoadenoma papillare, *Trudy klinik voronežskaro universiteta*, 2:125, 1927.

47. Gagucan, M.: Des tumeurs vésicales, *J. d'urol.* 24:469, 1927.

Foreign Bodies.—Wolff⁶¹ reported two cases of foreign bodies in the bladder; in a young girl, a hairpin was found, and in a middle-aged man a piece of chewing tobacco.

The diagnosis of foreign bodies can usually be made from the history. The symptoms are usually those of cystitis. Cystoscopically, besides foreign body, the mucous membrane of the bladder is diffusely red and the blood vessels are infected.

Treatment may be either conservative or radical, depending on the circumstances.

PROSTATE

Hypertrophy.—Hunt⁶² stated that the combined efforts of surgeon and clinician are more essential in the treatment of diseases of the prostate than of most other diseases. Serious organic disturbances are sometimes associated with prostatic obstruction, and, although the obstruction may be the first consideration, the coincident organic disease must also be considered in the care of the patient.

One of the most important coincidental conditions met is cardiovascular disease. Willius reviewed the records in 705 cases of enlarged prostate and noted cardiovascular disease in 42 per cent. Arteriosclerotic disease occurred most frequently (43 per cent). Arteriosclerosis associated with hypertension occurred in 36 per cent. In 8 per cent of the cases, angina pectoris was present. The incidence of cardiovascular disease is higher with prostatic obstruction than with many other diseases during the same decades, suggesting that coexisting cardiovascular disease is aggravated by persistent urinary retention.

The frequency of this association emphasizes the necessity for careful examination of the heart in all prostatic cases. Electrocardiographic studies are indispensable. Prostatectomy should not be performed in the presence of malignant hypertension, except under unusual circumstances. Most such patients live less than two years, and only 10 per cent live five years.

Renal complications must also be dealt with in the treatment of prostatic obstruction. The most common complications are insufficiency and infection; the latter is unquestionably a contributing factor in the production of the former. With drainage of the bladder and adequate treatment, the infection usually subsides. It often reappears after prostatectomy, especially when the preoperative treatment has been inadequate or too brief, and it may be the cause of death.

61. Wolff, E. P.: Zur Kasuistik der Blasenfremdkörper, *Ztschr. f. urol. Chir.* 23:428, 1927.

62. Hunt, V. C.: Reduction of Mortality Rate in Benign Prostatic Hypertrophy, *J. Iowa State Med. Soc.* 18:86, 1928.

are much more satisfactory. The best results have been observed in the treatment of papillomatous tumors. Gagucau believes that surgical treatment still gives the best chance for cure, especially in cases of malignant tumor. Combination of surgical treatment with cautery and radium increases considerably the chances of success in the treatment of infiltrated carcinoma of the bladder.

Cassuto⁴⁸ reported a case of pyonephrosis resulting from obstruction to the lower part of the ureter. The patient had had urethritis for two years and occasional attacks of hematuria and pyuria. Cystoscopic examination revealed a papilloma about 3 cm. in diameter on the edge of the right ureteral orifice and closing it almost entirely. The tumor was destroyed by fulguration. One month afterward, the symptoms still continued. A right pyelogram revealed extensive pyonephrosis; drainage was instituted.

Herman⁴⁹ reported a case of neoplasm of the trigone of the bladder. The patient, a man, aged 70, gave a long history of urinary disturbance, including dysuria, difficulty and a small stream. Hematuria had been present for six months. The results of the general examination were negative. Rectal examination did not reveal enlargement of the prostate. It was impossible to pass a cystoscope because of an intravesical mass. A water-dilating cysto-urethroscope revealed a normal urethra and vesical neck, and a mass in the trigone, which was lobulated and sessile.

At operation, a lobulated tumor was found occupying practically the whole trigone, with its major portion beneath the trigone. The overlying thin mucosa was incised in the long axis and was found to be friable in the region of the anterior declivity of the tumor. Immediately beneath the mucosal covering, a multilobular, well encapsulated, yellowish-white mass was exposed. This consisted of a number of individual lobules loosely bound together but well encapsulated as a whole. The gross appearance of the tumor was characteristic in miniature of hypertrophic prostatic tissue. The mass was about 3.75 cm. in the anteroposterior diameter, and 2.5 cm. slightly below the level of the trigone in its greatest width from side to side. Approximately 1.75 cm. of the mass projected above the trigone; the remaining 2 cm. was buried within and below the trigonal musculature. The main portion of the mass, comprising about two thirds of the growth, was deeply placed and well encapsulated so that it could be shelled out with surprising ease. There was considerable bleeding from the right anterior

48. Cassuto, A.: Uro-pyonéphrose due à un papillome implanté sur le méat urétéral, *Lyon. chir.* 24:253, 1927.

49. Herman, Leon: Neoplasm of the Trigone Vesicae: a Probable Instance of Hypertrophic Changes in Aberrant Prostatic Tissue, *J. Urol.* 19:291, 1928.

Experience has shown that the patient with prostatic obstruction is, as a rule, a poor subject for immediate operation. In 1925, 1,783 cases were reviewed in which suprapubic prostatectomy was performed at The Mayo Clinic between Jan. 1, 1913, and Jan. 1, 1925, with an average mortality of 5.5 per cent. The deaths occurring after prostatectomy were studied to determine the relationship between preoperative preparation and the mortality rate. It was shown that when patients, apparently in good general health and showing few, if any signs of renal injury were operated on immediately without preparation, there was a mortality rate nearly as great as in the group of patients in poor general health with marked renal insufficiency and infection, operated on only after adequate preparation. It has been three years since preoperative treatment has been instituted in all cases previous to prostatectomy at The Mayo Clinic. Before that time 37 per cent of patients, because of apparently good health and what appeared to be adequate cardiovascular renal reserve, were considered good subjects for the one-stage operation without any preliminary treatment. However, 44 per cent of the deaths after prostatectomy occurred in this group, and the mortality rate was 6.6 per cent. During the same period, 437 patients (24.6 per cent), considered the poorest subjects for operation, were treated by preliminary cystostomy and were adequately prepared before prostatectomy; the mortality rate in this group was 7.5 per cent. The remaining 38 per cent of patients, those with moderately impaired cardiovascular renal reserve, were treated by the installation of a permanent indwelling catheter until they were believed to be ready for operation. The one-stage suprapubic operation was used, and the mortality rate was 3.3 per cent.

The mortality rate is markedly influenced by the amount of preliminary treatment. During a period of one year in which preoperative treatment for a minimum of ten days was adopted in all cases, the following data were obtained: In 225 cases, there were 6 (2.3 per cent) deaths. A one-stage operation was performed in 188 cases with 4 deaths, a mortality rate of 2.1 per cent, as against a two-stage operation in 67 cases with death in 2, a mortality rate of 2.9 per cent.

Hunt stated that prostatectomy should never be performed without a period of preliminary treatment. In the majority of cases, satisfactory drainage can be obtained by a permanent indwelling urethral catheter. Vesical lesions, such as stones, diverticula and malignant tumors, associated with reduction of cardiovascular renal reserve, requiring a long period of preparation, still require cystostomy. Usually about 75 per cent of patients may be prepared by drainage through the urethral catheter.

Ether as a general anesthetic presents the greatest hazards in cases of prostatic obstruction, not in the administration, because it has a

segment of the bed of the tumor. This was controlled by packing and sutures, the latter being so placed that the interureteric bar was drawn forward to the trigonal mucosa. As the latter was necrotic and the underlying muscles atrophic, it was with some difficulty that the sutures were made to hold. The bed, on exploration bimanually, was found to be extensive, situated well above the prostate gland and sphincteric area, and to extend backward to the rectal wall, separated from the latter only by the capsule of the tumor.

The bladder was closed with drainage. Convalescence was uneventful for thirty-one days; the wound had closed with reestablishment of normal voiding. After the patient had been up for a week, he suddenly became stuporous and died in uremic coma within a period of twelve hours. The pathologic report on the tissue removed was "benign hypertrophy of the prostate gland."

There would not seem to be any question of the identity of the tumor, although certain vesical tumors classified as adenomas resemble in minute structure benign prostatic hypertrophy. The neoplasm apparently originated within or beneath the trigonal structures, and in its fully developed state was situated above the prostate gland, and at a considerable distance from the internal sphincter muscle. The normally situated prostate gland was not enlarged, and the position of the tumor and of the cavity from whence it came justified the conclusion that the tumor and the prostate gland were entirely unrelated anatomically. The question seemed to resolve itself into a differentiation of tumor originating from glandular tissue other than that comprising the prostate gland, of accessory glands in the region of the vesical outlet, and of benign hypertrophic changes in aberrant prostatic tissue.

Comparison with the growth and development of tumors known to have originated in the trigonal mucosal glands justified the conclusion that this tumor did not originate in these structures, but, in all probability, in structures beneath or within the trigonal musculature. The probabilities are that the tumor presented hypertrophic changes in aberrant prostatic tubules.

Deming⁵⁰ noted in the literature the reports of nine cases of primary carcinoma developing in diverticula of the bladder and reported one case of his own.

The age incidence in carcinoma and diverticula was between 57 and 70 years, most of the patients being close to the age of 62. All patients were men. All but one of the diverticula were infected. The diverticula were single; five were on the left side near the left ureteral orifice,

50. Deming, C. L.: Primary Carcinoma of Diverticulum of the Bladder, *J. Urol.* 18:73, 1927.

wider margin of safety than have other general anesthetics, but in the subsequent renal depression and acute pulmonary complications. Patients at the age when prostatectomy is usually performed are susceptible to the inhalation type of pneumonia and to bronchial troubles. Gas anesthetic, when skillfully administered, is usually satisfactory. Regional anesthesia minimizes the postoperative renal depression and pulmonary complications.

The successful management of prostatic obstruction necessitates regarding it from a general medical point of view as a systemic disease, not only by the urologist and the surgeon, but by the internist. The surgical principles involved in prostatectomy are significant, but so far as mortality is concerned Hunt believed that a poor operation after thorough medical and urologic consideration and adequate preoperative preparation is better than a skilful operation without preparation.

Ponce de Leon⁶³ favored deep roentgen-ray treatment in prostatic hypertrophy. He believed that if the prognosis is good, prostatectomy should be performed in every case. If the prognosis is poor, roentgen-ray treatment should be used. He does not limit roentgen ray to the treatment of hypertrophy, but cited four patients with chronic retention and vesical distention who were definitely benefited. He expressed the belief that radiocystitis will not result and that the blood urea content is not increased. Patients for roentgen-ray treatments must be as suitably prepared as for operation, so as to eliminate the possibility of uremia. Deep roentgen-ray treatment increases the difficulty of later enucleation. He felt that it does not enhance the change of adenoma to carcinoma (as believed by Legueu), and if all other specimens of operative cases were carefully sectioned, the same percentage of malignant lesions as found after radiation could be demonstrated.

Ponce de Leon reported a case of a patient, aged 74, whose preoperative diagnosis was adenoma. During the first operation, a hard knot was felt in the prostate gland and biopsy revealed adenocarcinoma. For this reason, and also because of the patient's poor health, deep roentgen-ray treatment was substituted for the second stage of prostatectomy with marked improvement. The author stated that had the roentgen ray been used first it would have been blamed for the carcinomatous change.

Gamissans⁶⁴ wished to refute Legueu and Compar, who in sixty cases of prostatic hypertrophy in which radiotherapy was used found only slight early decongestion. He stated that the latter is false, since, on the contrary, radiotherapy may start with congestion and edema

63. Ponce de Leon, J.: Concepto urológico actual de la radioterapia profunda en el adenoma de la próstata (Replica). *Rev. méd. de Barcelona* 7:496, 1927.

64. Gamissans, Angel: La radioterapia en el adenoma prostático, *Rev. méd. de Barcelona* 7:483, 1927.

four near the right ureteral orifice, and one in the median line just behind the interureteric ligament. The size of the diverticula varied from 2.5 cm. in diameter to that of a normal bladder. The vesical walls were much thickened and hypertrophied. Marked inflammation of the mucosa of the bladder was present as a result of severe infection. The urine was foul and contained a large amount of mucus. The symptoms were dysuria and obstruction extending over periods of from four months to three years. Interval hematuria was the outstanding clinical feature. Frequency was present in all cases, and is probably accounted for by the infection and inflammation of the bladder. Retention occurred in several of the cases.

The diagnosis of this condition is impossible without cystoscopy. The symptoms do not distinguish it from prostatic obstruction and carcinoma of the bladder itself. A cystogram helps to make a diagnosis of diverticulum, but not of the indwelling tumor. The cystoscope may not even disclose the tumor unless it protrudes from the mouth of the diverticulum. Furthermore, the mouths of diverticula have peculiar sphincteric actions, so that unless the stoma of the diverticulum is observed at varying intervals or at different stages of the filling and emptying of the bladder, the condition might be easily overlooked.

The treatment has been for the most part an attempt at removal of the diverticulum. Targett gave the data from the necropsy in three of the ten cases here reported. In three cases reported by Judd and Scholl the diverticulum was excised, but in the fourth case the diverticulum was so adherent that excision was not attempted. Harris reported a case in which cystotomy was performed, but the extent of the growth prohibited resection. In Deming's case, resection was readily accomplished. Young reported the only cure in a case of a small diverticulum 2 cm. in width. The carcinoma was not infiltrating and had not metastasized at the time of operation.

Death occurred from twenty-five days to two years after operative procedures. According to Targett's report on three necropsies, infection, pyelonephritis and uremia were the immediate causes of death. Metastasis was noted in one of the cases reported by Judd and Scholl in the lymph nodes along the right internal iliac vessels, and in another case, there was a recurrence in the suprapubic wound after five months. In Deming's case, signs of local recurrence appeared between the bladder and the rectum eight weeks after excision; nodules in the liver were also found which were thought to be an extension of the process.

The carcinoma in Targett's case was epithelioma. In other cases, the growth was of a papillary nature. Microscopically, the section from Deming's case showed a tumor of a high degree of malignancy; the cells were angulated, reticular and contained many mitotic figures.

and therefore increase the difficulty which will subside after eight days and leave the patient improved. The cases indicated for radiotherapy are those of early prostatic hypertrophy with congestion, and chronic retention but without vesical distention, cases with only slight changes in the vesical neck and slight elongation of the prostatic urethra. The cases in which radiotherapy is contraindicated are those of chronic retention with vesical distention and marked changes in the neck of the bladder; these belong to the surgeon. Gamissans reported cases in which symptoms were not present for five years following treatment. He believed that radiotherapy does not increase the difficulty of enucleation any more than the duration of time in which other changes may take place. Finally, radiotherapy does not enhance the malignant degeneration of adenomas.

Thomas⁶⁵ outlined at length the various considerations that come into play in the management of prostatic lesions. The cystoscopic determination of the type of lesion, the amount of residual urine and the force with which the urine is expelled through the catheter, are all evaluated.

The estimation of the urea nitrogen of the blood and the excretion of phenolsulphonphthalein are the most commonly used tests of renal function by the majority of urologists. From 20 to 30 mg. of urea nitrogen in the blood are considered safe values, while values above 30 mg. for each 100 cc. are dangerous, if not prohibitive, for operation. Regarding the phenolsulphonphthalein output, definite values have not been determined. Thomas emphasized that an output of 10 per cent one week, 20 per cent the next, and 30 per cent the next is a better index for operative success than an output of 50 per cent one week and 35 per cent the next. An effort should be made to establish the stability of renal function. In cases with injury to the kidneys, reliance cannot be placed on a single test.

Thomas described what he has called the index of elimination. This index is computed by taking the ratio of the percentage output of the dye for the first and third cycles (twenty minutes each) of a one-hour period of major elimination. Normally, the ratio is 5:1 and the index is said to be 5. When the quantitative output for the first twenty-minute period is greater than, or at least equal to, that of the third period, retention of urea is not present and renal function is invariably demonstrated as excellent. Such cases are considered in the positive phase for operability. When the output for the first period is less than that for the third period, the index is obviously less than 1, the kidneys are injured and the patient is in the negative phase.

65. Thomas, B. A.: *Vital Factors in the Management of Prostatic Obstruction*, Ann. Surg. 86:563, 1927.

rigid, a dead space is left on the side on which the operation was performed and thus exudation is induced, which may invite infection. In the experiments it was noticed that the less lung tissue removed the greater the chance for complete recovery. The method of leaving a certain amount of lung tissue to be used as a reinforcement over the bronchus is of distinct advantage. The danger of rupture in this stump is obviated first by the ligation of the larger bronchioles and also by the pneumothorax on the side on which the operation was performed. Another precaution is the production of temporary or permanent paralysis of the phrenic nerve at the end of the operation. This lessens the chance for an inspiratory suction action within the stump. If a stump of lung tissue is left, the pleural surfaces are approximated and thus a thick pleural covering is induced at the site of the resection of the lung. The fibrosis that occurs in the lung tissue of the stump adds to the efficiency of the operation.

In the operations in which the whole lung is removed and the bronchus is left exposed, none of the foregoing factors can be mobilized as aids. Moreover, the circulation, the vagus and the heart are disturbed by the unnecessary additional handling of the bronchus and its contiguous structures. Often it was found difficult to try such methods in ligating and suturing the bronchus without going through all its walls. Even with a perfect technic, the operation is much more prolonged than in the procedure employed in the present experiments. With the use of the technic described, it has been possible to complete the operation in from eight to twelve minutes from the time of the incision in the skin till the complete closure of the wounds. Our results with this type of operation are not different from those of Bettman.¹⁰ The wall of the bronchus was found resistant, and the greatest difficulty has been in attempting to invert the stump.

CONCLUSIONS

The method described has been found satisfactory in experiments on the dog. It provides for a stump which eventually becomes strong and prevents any possibility of perforation of the bronchus. The method is simple, does not require any special instruments and can be finished in the shortest possible time. It provides for approximation of endothelial surfaces in a manner similar to operations on the gastro-intestinal tract or the blood vessels.

10. Bettmann, R. B.: Experimental closure of Large Bronchi: A Study of the Factors Concerned in Failure of Bronchi to Heal. *Arch. Surg.* 8:418 (Jan.) 1924.

ACUTE EMPYEMA

TREATMENT BY CONTINUOUS TIDAL IRRIGATION AND DRAINAGE
DEPENDENT ON NORMAL RESPIRATORY MOVEMENTS *

DERYL HART, M.D.

BALTIMORE

The closed method of drainage and irrigation of an empyema cavity offers many advantages, chief of which are: 1. The method is simple and easy of operation, the insertion of a tube through a trocar under local anesthesia requiring only a few minutes. 2. The pressure within the cavity can be released at any desired rate. 3. There is little care in the form of dressings. 4. The cavity is not continually sucking air. 5. So long as the junction of the tube with the wall of the chest is air tight, suction can be applied, thus reducing the pressure within the empyema cavity below the surrounding atmospheric pressure and thereby decreasing the size of the cavity by expanding the lung.

On the other hand, many arguments have been advanced against this method of treatment. The most important has been that the drainage is inadequate; the pus, which becomes thick, and fibrin collecting in the tube cause a damming up of the infected fluid within the chest. This results in an elevation of temperature, and necessitates the removal and reinsertion of the tube or considerable effort to dislodge the plug which causes the obstruction. Each blockage with a damming up of the pus delays convalescence, not only by the systemic effect of the absorption of toxins and bacteria, with the danger of septicemia and metastatic infection, but by the rapidly progressing positive pressure within the empyema cavity which delays the expansion of the lung, and at times goes so far as to increase the size of the cavity by pulmonary compression.

This positive pressure within the chest also causes the pus to dissect along the tube, which, in the absence of a bronchial fistula, is the only avenue of escape from the infected pleural cavity. The most favorable course is for the pus to reach the surface, soil the dressings and dissect from the wall of the chest the adhesive straps holding the tube in place. With the infection and sloughing of the tissues about the tube, it soon becomes so loose that the cavity can no longer be kept air tight; then one has none of the advantages of closed drainage, while the small opening is inadequate for open drainage. Only the unusual patient has gone for ten days to two weeks without having the tube changed or become loose, permitting air to leak in through the hole in the wall of the chest.

* From the Surgical Department of the Johns Hopkins University and Hospital.

By repeated determination and observation of such indexes of elimination, Thomas believed that an accurate estimate can be made of renal function in a much better manner than that offered by the usual method of total excretion.

In considering the cardiovascular system, Thomas noted particularly the blood pressure of his patients. In cases of low tension in which the systolic blood pressure is 110 or less, the diastolic must be more than 60. When the diastolic is less than 60, the systolic must be more than 110. In cases of high tension in which the systolic pressure is 180 or more, the diastolic must be less than 100; when the diastolic pressure is more than 100, the systolic must not be more than 175. It is emphasized that this is not alone pulse pressure in its usual sense, but rather pulse pressure with systolic and diastolic limitations.

The significance of the Wassermann test, the determination of the coagulation time of the blood and of the blood sugar are given appropriate attention. Anemia is frequently found and must be overcome in preoperative treatment. The nervous system comes in for consideration with the possibility of tabes, multiple sclerosis, etc., as complicating factors. Thomas reported cases in which the functional nervous disorder, uncontrollable fear of death, was an evil operative omen. Rarely will the pulmonary or gastro-intestinal symptoms present features which contraindicate operation, but usually any such symptoms may be overcome, especially if caudal and transsacral anesthesia are used. Age in itself is never prohibitive if the patient's organs can be brought to function properly.

Thomas favored suprapubic prostatectomy when the gland is greatly enlarged or when intravesical complications such as stone, diverticula, or trigonal hypertrophy exist. When the hypertrophy is confined to one or both lateral lobes or the gland is small, fibrotic and presumably adherent, undoubtedly it should be removed by the perineal route. Again, in the group of patients who have the bar or glandular type of obstruction, some form of punch operation or excision with the electric knife is indicated. Thomas advocated, in many such cases, the removal of orificial obstruction by means of the punch or rongeur, suprapubically, as it is more effective and thorough, and there is less danger from infection and hemorrhage than by the urethral route.

As indications for primary cystotomy and secondary prostatectomy rather than the one-stage operation after catheter drainage, Thomas named: (1) marked cystitis, (2) intravesical complication such as stone, tumor, clots, and so forth, (3) epididymitis, (4) stricture and some cases of false passage of the urethra, (5) unusually small or sensitive urethra, (6) unusually obstructive or impassable prostate and (7) febrile cases or catheter cases in which urethral fever and chill develop.

dissection along the innermost layer of tunic, infiltrating the lowest portion of the sac with anesthetic, if necessary to block the pudic nerves. The mass is then delivered through the wound and incised from end to end. The redundant tunica vaginalis is excised and complete hemostasis is obtained by a running suture in the tunica vaginalis if necessary. The remaining edges are everted and sutured behind the cord. Hemostasis is carefully watched and the testis is replaced in the scrotum. The wound is closed without drainage. A small gauze dressing and a special hemostatic bandage⁸⁰ are applied.

Complications, such as hemorrhage, infection, involvement of the testis, or recurrence of the condition, may ensue. Hematocele, if large, requires evacuation. Admonition as to the utmost care in asepsis is given. Scrotal edema may occur at times. Testicular involvement may be immediate in the form of traumatic orchitis or postoperative infection, and later there may be atrophy. In eight cases of this series, testicular involvement called for orchidectomy.

The average period in the hospital in this series was 9.3 days. Two patients died of bronchopneumonia following operations under local anesthesia.

Recurrence as quoted by Bruns was approximately 2.4 per cent. Campbell examined thirty-three cases of this series. In four a slight collection of fluid at the upper pole apart from the testis was noted. In two cases, there was definite recurrence. At the second operation it was found that two layers of the tunica vaginalis were glued together in the formation of a cyst, not involving the testicle but just above it.

[ED. NOTE.—This is an excellent review of a common and much neglected lesion. As Campbell pointed out, the procedure of choice is always open operation; recurrence of the condition is three times as severe after tapping and injection. The latter methods seem somewhat obsolete but it is sometimes necessary to consider them in individual cases.]

Varicocele.—Bate⁸¹ reviewed the literature on varicocele carefully. Petit was the first to describe varicocele as one of the symptoms of renal tumor. In 1881, Guyon and Morris gave clear accounts of cases of this condition. Bate reported fourteen cases of varicocele and renal tumor from the records of the Massachusetts General Hospital. From these he found that varicocele is a late sign and carries with it a poor prognosis. Only 28 per cent of his patients were temporarily relieved by operation. The condition is probably not often noted in early

⁸⁰. For description of this unique bandage reference is made to the original article (footnote 79).

⁸¹. Bate, J.: Symptomatic Varicocele, *J. Urol.* 18:649, 1927.

For an anesthetic, much depends on the case. An absolute rule is not given. In certain cardiovascular, renal and pulmonary cases spinal, regional, or other forms of local anesthesia, unquestionably should be used. Most patients, if properly prepared, stand general anesthesia under gas or even ether well, much depending on the efficiency of the anesthetist.

Hemostasis is satisfactorily obtained with suture of the bleeding points at the time of operation. The use of the pneumatic bags of Hagner, Pilcher or Ballenger is advocated; packing of the prostatic fossa is the least desirable method.

Ligation of the vas as a preventive of epididymitis is regarded as unnecessary in most cases. Suction drainage is not used.

Postoperative care is held in equal importance with preoperative treatment. Sodium chloride and dextrose solutions, diuretics and cardiac tonics, especially digitalization, save many lives. The importance of vesical irrigations in the presence of infection and of general hygiene of the bladder in the prevention of pyelitis and pyelonephritis is emphasized. These old men should not be forced out of bed too soon. Many complications of epididymitis and a few of phlebitis and embolism will thereby be avoided.

[ED. NOTE.—While there are details with which some may disagree, Thomas has reviewed many features of handling prostatism which show experience and sound judgment. His description of the value of determining an index of elimination, his evaluation of blood pressure readings and his indications for the two-stage procedure are particularly appealing and seem worthy of practicing. It is to the credit of urology as a specialty that a low operative mortality has been achieved in what appears to be and has been the poorest sort of surgical risk. The low mortality rate has been the result of the many improvements in operative technic and the conscientious and detailed physiologic and biochemic studies during the periods preceding and following operation.]

Lowsley and Harrah⁶⁶ reported the unusual case of a man, aged 32, who had had urinary obstruction due to prostatic tumor for three months and was admitted to the hospital with complete urinary retention. Catheter drainage and preliminary care were followed by cystoscopy, which revealed enlargement of the prostate. Suprapubic cystostomy was performed at which time a piece of the tumor was removed for examination. Fourteen days later, the prostate was

66. Lowsley, O. S., and Harrah, F. W.: Enlargement of the Prostate Gland with Characteristics Resembling Hodgkin's Disease: Malignant Granuloma, *Ann. Surg.* 86:556, 1927.

examinations because the patient is examined while recumbent. Thrombosis and tumor in the left renal vein occur with and without varicocele and are probably significant etiologic factors. Enlarged lymph nodes were recorded in one of the cases in which operation was performed. Pressure from the tumor would account for the varicocele in several cases.

Although many writers refer to varicocele as a symptom of lesions other than malignant tumor, the records of the Massachusetts General Hospital do not bear this out. One case was reported from the literature, in which varicocele occurred with severe pyonephrosis. Although symptomatic varicocele is a late sequel and carries with it a poor prognosis, in properly selected cases the chance for temporary relief should not be denied the patient merely because symptomatic varicocele is present. When a suddenly developing varicocele is noted in a patient of advanced age, renal tumor should be considered. Varicocele occurred in 20 per cent of the cases of hypernephroma and in 11 per cent of all malignant tumors of the kidney; it was the presenting symptom in 30 per cent of Bate's cases.

Epididymitis.—Wade,⁸² in discussing treatment, divided vaso-epididymitis into five stages according to clinical symptoms and pathologic manifestations.

In the first stage the patient usually presents himself complaining of pain in the groin and along the course of the vas deferens; there is a general feeling of malaise, which indicates that vasitis is present and the descending infection will soon involve the epididymis. The patient is immediately put to bed without further local treatment to the urethra or prostate, ice is applied to the painful area and 15 grains (0.972 Gm.) of calcium chloride is administered intravenously. This is repeated daily until the pain disappears. At this stage, a vas puncture with injection of the seminal vesicle on the affected side can be done satisfactorily. This is an attempt at abortive treatment.

The second stage is that in which the epididymis has become involved; there is slight swelling, tenderness and pain along the course of the vas deferens, and general malaise. Such patients also are sent to bed; calcium chloride is given daily intravenously; the scrotum is elevated and cold applications are applied. Diathermy may be used to good advantage. The epididymitis may subside at this stage or it may pass into the third stage.

In the third stage, there is considerable enlargement of the epididymis and all the symptoms are much more severe than in the previous stage. In some of these cases Wade expressed the belief

82. Wade, H. K.: Treatment of Acute Gonorrheal Epididymitis with Special Attention to Prevention of Azoospermia, *J. Urol.* 18:427, 1927.

removed under regional anesthesia. At one point the prostate had infiltrated the prostatic capsule and malignancy was suspected. Microscopic examination of the growth showed newly formed granulomatous tissue, rich in plasma cells and containing mononuclear giant cells suggestive of the Sternberg type, and eosinophilic leukocytes. An inguinal lymph node, removed for section, showed simple chronic lymphadenitis.

The microscopic picture suggested a granuloma of the type of Hodgkin's disease and relative lymphocytosis. However, other features of Hodgkin's disease, which are carefully outlined by the authors, were wanting.

The unusual condition of complete urinary retention due to solid prostatic tumor in a patient, aged 32, is emphasized; a case of the kind had not been reported previously. The gradual onset of symptoms exhibited by the patient is similar to those described in most cases of adenomatous enlargements of the prostate in old men. The usual and frequent painful urination culminated in complete retention of urine rather more rapidly than in most cases of adenoma.

[ED. NOTE.—The histologic picture presented is even more uncommon than the rarity of prostatic obstruction in early adult life. Sarcoma of the prostate occurs much earlier and cancerous neoplasm much later than the age of 32. Furthermore, Hodgkin's disease rarely affects the prostate. Tuberculosis, a condition at times confused with Hodgkin's lymphadenitis, was considered but none of the features of tuberculosis was present. Unfortunately, the follow-up record of the patient is not mentioned. This might reveal further interesting information in this most rare clinical and pathologic picture.]

Leguen⁶⁷ reported a number of cases of hypertrophy of the vesical neck. The hypertrophy involved not only the fibromuscular and glandular tissue, but also all the other tissues which comprise the vesical neck. Usually symptoms of retention are present over a long period. Leguen considered the glandular hypertrophy as a mild type of prostatic disease. In prostatic disease various types of adenoma may be found. There may be adenomas which weigh only a few grams, some that are barely perceptible to the eye and others so small that only the microscope can establish their existence. Functional symptoms are more marked and appear earlier in fibromuscular hypertrophy than in glandular hypertrophy. At times these hypertrophied areas contain histologic signs of secondary infection. Excision of the neck of the bladder is the best treatment for this condition.

67. Leguen: L'hypertrophie du col vésical, Bull. Soc. franç. d'urol. 6:222, 1927.

that he is justified in prescribing rest and using the expectant treatment outlined, but in many cases the Hagner operation should be performed.

In the fourth stage, the epididymis is enormously enlarged with more or less severe orchitis and hydrocele. The temperature is elevated and leukocytosis is marked. The patient is toxic and suffers intensely. In all such cases, the radical or surgical method should be carried out early.

Azoospermia can be prevented in a large percentage of cases by a carefully performed epididymotomy in selected cases.

Gurewitsch⁸³ discussed two cases of gonorrheal funiculitis. Clinically, the symptoms were peritoneal and suggested the diagnosis of strangulated hernia. In both cases the aponeurosis was split down to its lowermost layer to obviate any stasis, and the entire funiculus freed in layers. Closure was then carefully made, and healing occurred in eight days. Hernias did not result. According to Gurewitsch, operation hastened healing.

Urogenital Tuberculosis.—Marion⁸⁴ has performed 1,267 operations for genital tuberculosis since 1908. He has found the testis affected in about a tenth of these cases. In the remainder, the infection was localized to the epididymis.

Epididymectomy, which is more difficult to perform than nephrectomy, is possible even in advanced cases. In order to prevent the formation of fistula, Marion divides the vas and fixes it to the skin. The wound is left partly open. Cicatrization usually proceeds rapidly. He considers general postoperative treatment, such as good air, sunlight and ultraviolet lights, important. He also uses so-called antigen of Negre and Bouquet (apparently a tuberculin treatment), prepared at the Pasteur Institute. Castration is performed only as a last resort.

Wildbolz,⁸⁵ in discussing the treatment of urogenital tuberculosis, stated that he has obtained satisfactory results by epididymectomy combined with general postoperative treatment. More than 60 per cent of his patients were definitely cured, while 20 per cent died of pulmonary, renal, or other forms of tuberculosis. In order to save the testis, Wildbolz recommended early epididymectomy as the treatment of choice in cases of acute epididymitis.

Choltsoff⁸⁶ stated that tuberculosis of the prostate and vesicles usually accompanies tuberculosis of the epididymis. Isolated tuber-

83. Gurewitsch, G. M.: Zur chirurgischen Behandlung gonorrhöischer Funiculitiden, *Zentralbl. f. Chir.* 54:1225, 1927.

84. Marion: Traitement de la tuberculose génitale chez l'homme, *J. d'urol.* 24: 358, 1927.

85. Wildbolz: Traitement de la tuberculose génitale chez l'homme, *J. d'urol.* 24:357, 1927.

86. Choltsoff: Tuberculose uro-génitale, *J. d'urol.* 24:464, 1927.

Kreutzmann⁶⁸ noted that although hydro-ureter and hydronephrosis have long been associated with obstructive urethral lesions the mechanism of formation of the dilatations is still an open question. His investigations have demonstrated that ureteral reflux is not common in obstructive lesions of the vesical neck and urethra. Reflux usually is unilateral and dilatation of the ureter and renal pelvis has even been demonstrated on the intact side.

Kreutzmann expressed the opinion that his investigations tend to substantiate Tandler and Zuckerhandl's theory that the dilatation of the upper part of the urinary tract is due to the vas deferens. Kreutzmann concluded that (1) in cases of hypertrophied prostates, hydro-ureter and hydronephrosis may occasionally occur as a result of the kinking of the ureters by the vas deferens; (2) the most common cause of dilatation of the upper part of the urinary tract in obstructive lesions of the vesical neck and urethra in adults is constriction of the intramural portion of the ureter; (3) this constriction is due to hypertrophy of the musculature of the bladder surrounding the ureters; (4) reflux is not common in these conditions, and when present, it is caused by an infection in the ureter resulting in a stiffening of its intramural portion, and (5) reflux is a terminal and not a primary phenomenon of prostatic hypertrophy and urethral stricture.

Alyea⁶⁹ pointed out the high incidence of epididymitis in cases of prostatic obstruction. This incidence is reported by White of London as 82 per cent, which is an unusually high percentage as White included many cases of slight induration as true epididymitis. From other reports, it would appear that about 40 per cent is a correct estimate of the occurrence of this complication.

Alyea pointed out the practical importance of preventing both preoperative and postoperative epididymitis in cases of prostatic obstruction. Statistics from various clinics emphasize the far too frequent occurrence of this complication. The advance in methods for its prevention was traced through seminal vesiculectomy, ligation of the ejaculatory ducts, to ligation of the vas in the scrotum by a closed method. It is demonstrated that the time for ligating is not at the operating table after the patient has already been handicapped by present or latent epididymitis, but at the time of his admission to the hospital, before urethral instrumentation or the insertion of a retention catheter. This is strongly advised for adoption as a ward routine in all cases of prostatic obstruction. To make this practicable, he has

68. Kreutzmann, H. A. R.: *The Cause of Renal Back-Pressure in Obstructive Lesions of the Urethra and Bladder Neck*, J. Urol. 19:199, 1928.

69. Alyea, E. P.: *Vaso-Ligation a Preventive of Epididymitis Before and After Prostatectomy*, J. Urol. 19:65, 1928.

culosis of the prostate might sometimes occur, but isolated tuberculosis of the vesicles is never seen. Epididymectomy is indicated in advanced cases or in cases in which the disease is progressing rapidly. If a portion of the testis is also infected, this part should be removed. Epididymectomy and orchidectomy favorably influence prostatovesicular tuberculosis. In advanced cases, it is necessary completely or partially to remove these organs. The perineal route is usually the more desirable one.

Abricosoff⁸⁷ stated that in the majority of cases tuberculosis of the urogenital system develops from hematogenous metastasis from a primary pulmonary focus.

URETHRA

Tumors.—Wurmser⁸⁸ stated that carcinoma of the urethra is observed in the perineoscrotal, penile and balanic urethra in decreasing frequency. Two significant elements in the etiology seem to be chronic gonorrhea and the transformation of urethral polyps. Carcinoma of the glands and of the balanic urethra both develop from squamous epithelium. In the deep urethra the cells are of the cylindric type. Metastasis is common, especially to the lungs. Disturbances of micturition are usually the first symptoms; others are tumor, pain, hematuria, discharge, fistulas and adenopathy. The diagnosis and differential diagnosis are thoroughly discussed. Death in from six months to one year is the usual result in untreated cases.

[ED. NOTE.—Usually carcinomas in the posterior urethra of the male, although developing on a cell that is somewhat cylindric, infrequently have squamous cell characteristics. Some of the cases reported by Wurmser were of short duration and death occurred shortly after the first appearance of trouble. In several cases reported by other observers, the appearance of the carcinoma was preceded by long periods of urinary difficulty and irritation. The tumor formation is somewhat analogous to the long standing premalignant stages preceding the development of squamous-cell tumors of the urinary bladder. König reported a case of urethral carcinoma developing after urinary obstruction of forty-eight years' duration, and Oberlander noted a somewhat similar case developing after forty years of urinary difficulty. Infection is unquestionably an important factor in the formation of these urethral growths. Infection usually progresses to the point of stricture and the malignant changes come later. Traumatic strictures also have the same malignant potentialities as those of infectious origin. The majority

87. Abricosoff: Tuberculose uro-génitale, *J. d'urol.* 24:463, 1927.

88. Wurmser, Raymond: L'épithélioma primitif de l'urètre périnéal chez l'homme, *J. d'urol.* 24:497, 1927.

described in detail the technic of vasoligation through the skin, without an anesthetic, which is done in bed or in the ward treatment room. At the Brady Urologic Institute, the vas has been ligated in fifty cases of prostatectomy⁷ according to the procedure, and the percentage of occurrence of epididymitis is four. They believe, therefore, that if this regimen is adhered to rigidly the occurrence of preoperative as well as postoperative epididymitis in the treatment of prostatic obstruction can be practically eliminated.

[ED. NOTE.—Many urologists are now employing some type of vasoligation as a routine. If done early enough, this simple procedure usually prevents epididymitis and in some cases it may save life.]

Scott⁷⁰ reviewed the dangers of rapidly emptying the chronically overdistended bladder and the various methods of decompressing such bladders more slowly. According to his observations, the best results are obtained by taking a relatively short time to empty the bladder, namely, about twenty-four hours. To accomplish this, he has successfully used an ordinary olive-tipped ureteral catheter. Decompression by means of a ureteral catheter has been used only as an emergency measure in his clinic. It has been of special value in those cases of carcinoma of the prostate in which the lumen of the prostatic urethra was so markedly decreased in size that it was impossible to pass anything larger than a filiform. In such cases the ureteral catheter also acts as a dilator, and it is possible, by inserting larger catheters every two days, to dilate the urethra rapidly so that a soft rubber catheter can be passed within a short time. The method also proved to be satisfactory in the case of a small boy having acute paradoxical incontinence due to the presence of a congenital urethral valve.

Because of the satisfactory results obtained by the apparatus now in use for decompressing the bladder in the presence of retention due to simple benign prostatic hypertrophy, the ureteral catheter has not been used in such cases. However, there does not seem to be any good reason why this method could not be used if decompression of the bladder is otherwise impossible.

Tuberculosis.—Bothe,⁷¹ in searching the literature, found only nine cases of tuberculosis of the prostate gland without demonstrable coincident tuberculosis elsewhere in the genito-urinary tract, and to these he added a tenth case. In four of the cases, the prostate had undergone hypertrophy. His case presented the usual signs and symptoms of benign adenomatous hypertrophy of the prostate. Pros-

70. Scott, W. W.: Gradual Decompression of the Bladder with a Ureteral Catheter. *J. Urol.* 19:81, 1928.

71. Bothe, A. E.: Primary Tuberculosis of the Prostate, *J. Urol.* 18:494, 1927.

of carcinomas which follow long standing infection and trauma occur in men of the cancer age and commonly occur at the usual site of stricture formation in the cavernous and membranous urethra. Occasionally they occur in the penile urethra, but rarely in the fossa navicularis. Of forty-two cases of carcinoma of the male urethra reviewed by Preiswerk, thirty-eight were in the membranous or cavernous urethra. Wurmser stated that metastatic growths are common, but it has been the experience of other observers that metastasis only occurs in the later stages. When secondary deposits occur they have the same tendency to remain localized in the primary glands as do those arising from epitheliomas of the penis. In young men, carcinoma is more likely to be papillary than squamous cell, and the long premalignant period of trauma and infection is generally absent. Papillary carcinomas in most reported cases were extremely malignant; they rapidly infiltrate the surrounding tissues and metastasize freely. Hutchison reported a case of a man, aged 22, with papillary carcinoma of the urethra; ulceration through the body of the penis occurred three weeks after the onset of swelling and obstruction. Six weeks after the first symptoms the regional glands were involved.]

Epispadias.—Sexton⁸⁹ stated that epispadias in women rarely occurs. Lower noted only forty-three cases in the literature up to 1922. He added one to the number. Sexton reported the case of a woman, aged 27, with marked separation of the labia minora and labia majora, rudimentary clitoris, an intact urethral sphincter and diastasis of the symphysis, but not associated with incontinence. Treatment was not attempted.

Priapism.—McKay and Colston⁹⁰ stated that true persistent priapism is rarely noted. Hinman had reviewed 170 cases up to 1914. They searched the literature carefully and found 22 others, making the total 192 cases. It was noted that if the erection persists for two days or more thrombosis is present in the corpora which in itself is sufficient to sustain the erection. Hence, if the underlying cause is treated successfully the erection will persist until the clot in the corpora is disposed of either by absorption or by evacuation. The immediate relief of the patient's symptoms depends on the collapsing of the penis by emptying it of this clot. It is, therefore, advocated that the erection be first relieved and the etiologic factor treated later. Various medical measures have been utilized. The use of sedatives, narcotics and hypnotics are usually of no avail. Deep anesthesia has been tried, and spinal

⁸⁹ Sexton, W. G.: Epispadias in Women: Case Report, *J. Urol.* 18:663, 1927.

⁹⁰ McKay, R. W., and Colston, J. A. C.: Priapism: New Method of Treatment, *J. Urol.* 19:121, 1928.

tatectomy was performed. On microscopic examination of the removed gland, a tuberculous focus was found. Other evidence of tuberculosis was not found. Tuberculosis of the genito-urinary tract forms about 5 per cent of all tuberculous cases found at necropsy and evidence of pulmonary tuberculosis is frequently found associated with genito-urinary tuberculosis. The prostate is frequently the seat of an associated tuberculous lesion when the other genito-urinary organs are primarily infected, but tuberculosis of the prostate, as a primary lesion in genito-urinary tuberculosis, is exceedingly rare. Hypertrophy may follow a tuberculous lesion of this gland.

[ED. NOTE.—Primary tuberculosis of the prostate is a rare condition. Grossly, it sometimes resembles carcinoma, particularly after the specimen has been removed, hardened and sectioned. Clinically, other symptoms of urinary infection usually distinguish this condition from malignancy. With secondary tuberculosis, the prostate usually becomes hard, small, fibrous and slightly nodular.]

Prostatic Secretion.—McCarthy⁷² and his associates reported data regarding the chemical composition of the prostaticovesical secretions of normal young men. These secretions contain an unusually high concentration of calcium, inorganic phosphorus, "hydrolyzable" phosphorus and amino nitrogen. It is believed that the amino nitrogen and hydrolyzable phosphorus may be partly in the form of spermin.

The sugar concentration showed marked variations. The sugar content of fresh semen greatly exceeded that of blood. Glycolysis was observed during incubation of the semen at 38 C. for from nine to twelve hours. The decrease in sugar was accompanied by a rise in lactic acid. However, the amount of lactic acid formed does not account for all of the sugar lost. It is probable that glycolysis is a phenomenon attributable to living spermatozoa, and that the lactic acid is an intermediate product in the utilization of sugar.

A study of the hydrogen-ion concentration of the semen during glycolysis demonstrated an efficient buffer mechanism in this fluid.

TESTIS AND EPIDIDYMIS

Tumors of Testis.—Morris⁷³ gave a general discussion of the present status of the theories and classification of testicular tumor. Ewing stated that all tumors are teratomas; Chevassu maintained that there are two classes of testicular neoplasms differing essentially in cell mor-

72. McCarthy, J. F.; Stepita, C. T.; Johnston, M. B., and Killian, J. A.: *Biochemical Studies of Prostato-Vesicular Secretions*, J. Urol. 19:43, 1928.

73. Morris, J. H.: *Malignant Tumors of the Testicle with Special Reference to Classification*, Arch. Surg. 15:530 (Oct.) 1927.

anesthesia in early cases. The latter should be effective provided thrombosis has not set in.

Surgical treatment is carried out as follows: (1) radical amputation if the erection is sustained by the presence of a local malignant neoplasm; (2) ligation of the dorsal arteries; (3) division of the ischiocavernosus muscles in the perineum and the arteries and nerves that pass through them, and (4) incision into the corpus cavernosum and evacuation of the contents of both sides.

McKay and Colston reported three cases with favorable results. They advocated and used the method of aspiration of the corpora, under local anesthesia. This procedure can be repeated several times if priapism returns.

McKay and Colston concluded that the easiest method of evacuating the blood clot in the corpora is by aspiration. It may be done with minimal danger. There are no contraindications to its frequent employment if necessary. The method of aspiration produces much less trauma to neurovascular mechanism producing erection than more radical surgical procedures, thereby enhancing the probability of subsequent normal erections.

phology and histogenesis: (1) embryonal, distinguished by their heterologous, atypical structure and embryonal origin, and (2) the simple, homologous, unicellular growths arising from fully differentiated adult tissues. Because of the controversial nature of the field, a case was reported which was of especial interest since embryonal adenocarcinoma and seminomatous tissue were found coexisting. Morris, therefore, concluded that: (1) the large cell tumor of the testis is of the embryonal type, (2) the theory of invariable unicellular or homologous nature is herein disproved and (3) the evidence adduced from this case substantiates Ewing's theory of teratomatous origin.

[ED. NOTE.—The evidence is slowly gathering in favor of Ewing's theory of the teratomatous origin of malignant testicular tumors. Universal acceptance of this theory would tend to end the confusion which characterizes the classification. Although the classification of testicular tumors has been greatly simplified through the classic investigations of Wilms, Ewing and others, two opposing schools have arisen, one maintaining that "for practical purposes there exists only tumor of the testis, namely, a teratoma" (Ewing, O'Crowley and Martland, Wilms, Pick, Ribbert) and the other, that besides the teratomatous group, there is a large proportion of testicular neoplasms which are purely homologous or single cell tumors (seminomas) derived from the cells of the spermatic tubules (Chevassu, Frank, Schultz and Eisendrath, Sakaguchi, Vecchi, Geist and Thalheimer, Hardonia and Patel). The recording of such reports as those of Morris and Hinman, Gibson and Kutzmann will in time effect a reconciliation of these opposing schools and eradicate much of the confusion in their classifications. The teratoma of the testis is a tumor of tridermal origin, and the unicellular type of tumor, such as the seminoma, can be considered an overdevelopment of one tissue in a tridermal growth. Hence the term "teratoma testis" should be used inclusively, and, as such, signify all types of degeneration. It is well to remember that in general the malignant elements in mixed tumors are almost uniformly epithelial and therefore carcinomatous in nature, and that these carcinomatous elements in the teratoma are generally amenable to classification into one or more of three groups: (1) trophoblastic (chorio-epithelioma), (2) hypoblastic (adenomatous type), and (3) epiblastic (solid alveoli of basal cell type and tumors of the neurocytoma group)].

Proust⁷⁴ reported two cases of seminomatous tumors of the testicle observed by Proust and Mallet in 1922, in which rapid absorption was obtained with hard roentgen rays. In the first case there was a swelling

74. Proust, R.: *État actuel de la radiothérapie des séminomes*, Bull. de l'Assn. franç. p. l'étude du cancer 16:247, 1927.

INDEX TO VOLUME 17

| | PAGE | | PAGE |
|--|----------|--|----------|
| Abdomen, surgical significance of abdominal reflexes | 854 | Blood—Continued | |
| Abscess, paraneuritic | 884 | in cerebrospinal fluid, resultant functional and organic alterations in central nervous system | 18, 39 |
| Adenoma, chronic mastitis, cysto-adenoma and adenoma of breast | 535 | "stream line" phenomena in portal vein and selective distribution of portal blood in liver | 408 |
| Allen, A. W.: Bactericidal properties of solution S. T. 37 (liquor hexylresorcinolis 1:1,000) | 834 | vessels, blood supply to appendix | 577 |
| Amylase, fecal, pancreatic function tests; with special reference to quantitative determination of | 899 | vessels, diseases | 696 |
| Anastomosis: See Intestines, anastomosis | | vessels, ligation of artery and concomitant vein in operations on large | 244 |
| Anesthesia, in urethrography | 872 | vessels, venous abnormalities and angiomas of brain | 715 |
| Aneurysm, arteriovenous, of brain | 190 | congenital deformities | 525 |
| Angioma, and venous abnormalities of brain (so-called); arteriovenous aneurysm of brain | 715 | development of, in diabetic children | 1017 |
| Ankle, osteotomy of malleolus | 190 | ossification after fracture | 700 |
| Antiseptics, bactericidal properties of solution S. T. 37 (liquor hexylresorcinolis 1:1,000) | 706 | osteogenesis imperfecta | 813 |
| Aorta, terminal abdominal, ligation of | 834 | physiology of, in relation to diseases of bone tissue, in conditions of circulatory disturbance | 700 |
| Appendicitis, acute, trauma as factor in | 794 | Braasch, W. F.: Multiple renal stones; problems in treatment of patients with this condition | 526 |
| Appendix, blood supply to | 672 | Brain, arteriovenous aneurysm of | 259 |
| Arteries, arteriovenous aneurysm of brain; ligation of, and concomitant vein in operations on large blood vessels | 577 | venous abnormalities and angiomas of | 190 |
| Arthritis | 190 | causing obstruction | 715 |
| chronic, relation of surgical pathologic conditions of right lower quadrant to | 244 | Breast, chronic mastitis, cysto-adenoma and adenoma of | 440 |
| gonorrheal | 530 | Bronchopneumonia, postoperative, oxygen in treatment of patients with | 535 |
| O-dixybenzoic acid treatment for | 532 | Brooks, B.: Ligation of terminal abdominal aorta; an experimental study | 1047 |
| Ascariasis, of gallbladder | 533 | Brown, L. T.: Thirty-sixth report of progress in orthopedic surgery | 794 |
| Atelectasis: See Lung | 324 | Bucholz, H. C.: Thirty-sixth report of progress in orthopedic surgery | 521, 689 |
| Bacillus welchii, antitoxin, relation of, to toxemia of intestinal obstruction | 860 | Calcification, normal physiologic, of matrix in cartilage and in bone | 1017 |
| Back, pain in | 527, 876 | Calcium salts, problem of manner of deposition of | 1017 |
| Bagley, C. Jr.: Blood in cerebrospinal fluid; resultant functional and organic alterations in central nervous system; A, experimental data | 18 | Cancer, chronic ulcerative colitis associated with malignant disease | 561 |
| functional and organic alterations in central nervous system; B, clinical data | 39 | exstrophy of bladder complicated by carcinoma | 641 |
| Ball, R. P.: Bilateral lobar atelectasis; report of case with autopsy observations | 82 | of lower lip | 630 |
| Bargen, J. A.: Chronic ulcerative colitis associated with malignant disease | 561 | uterine carcinoma | 897 |
| Barron, M. E.: Simple, nonspecific ulcer of the colon | 355 | Cartilage, normal physiologic calcification of matrix in bone and in | 1017 |
| Basograph, graphic records of normal and pathologic gait | 701 | Cauda Equina: See Spinal Cord | |
| Binger, M. W.: Oxygen in treatment of postoperative bronchopneumonia | 1047 | Cerebrospinal fluid, blood in; resultant functional and organic alterations in central nervous system | 18, 39 |
| Bissell, A. H.: Trauma as factor in acute appendicitis | 672 | Charcot's Joints: See under Joints | |
| Bladder, contracture of neck of | 1057 | Cheate, G. L.: "Chronic mastitis," "cysto-adenoma," and adenoma of breast | 535 |
| decompression of | 344 | Christian, L. W.: Pancreatic function tests; with special reference to quantitative determination of fecal amylase | 899 |
| exstrophy of | 346 | Clamps, relative mechanical strength of enterostomies performed with and without clamps | 658 |
| fistula of, complicated by carcinoma | 1058 | Classification, graphic records of normal and pathologic gait | 701 |
| foreign bodies in | 1062 | limps caused by diseases of hip | 701 |
| gangrene of | 343 | premature ossification of lower epiphysis of tibia following forcible correction of clubfoot | 521 |
| lesions of nerves of | 1056 | Cohn, J.: Epithelial neoplasms of peripheral and cranial nerves; report of 3 cases; review of literature | 117 |
| paralysis of | 1062 | Colitis, chronic ulcerative, associated with malignant disease | 561 |
| syphilis of | 1061 | | |
| tuberculosis of | 1061 | | |
| turns of | 1061 | | |
| Black, A.: Ligation of terminal abdominal aorta; an experimental study | 794 | | |
| relation of ligation of terminal abdominal aorta to ligation of fractures of | 794 | | |

of the right leg, which was believed to be phlebitis, but which disappeared rapidly following radiotherapy. Since there have been similar cases, Proust assumed that the condition was due to obstruction of the lymph channels by carcinoma cells. In order to prevent the obstruction of the lymph channels and the formation of metastasis, soft rays were used which minimize roentgen-ray burns. In six cases of seminoma, the duration of life was lengthened fourteen, nineteen, thirteen and twelve months, and two patients are alive two and three years respectively since beginning treatment.

Pearlman⁷⁵ reported a case of torsion of an undescended abdominal testicle associated with malignancy. In patients, aged 18, undescended testicles are doubtless more prone to malignant change and torsion than are normally placed testes. Pearlman's case is of interest in that both conditions are seen in the one case.

Valdoni⁷⁶ stated that tumors of the genitals range as follows in the order of frequency: testis, epididymis, vas deferens, seminal vesicles and tunica vaginalis. He described a case of a small cell sarcoma of the dividing membrane of the scrotum in a boy, aged 17, which developed one and a half years after the scrotum had been injured by a hoof. Castration with complete extirpation of glands to the renal hilum was carried out. Metastasis occurred shortly afterward.

Chwalla⁷⁷ stated that sarcomas are the most common of tumors of the spermatic cord and lipomas are next in frequency. The literature, mostly French, reports about twenty-four cases. Chwalla reported a case of fibrosarcoma of the spermatic cord. The tumor was a rapidly growing spindle cell fibrosarcoma with giant cells and apparently originated either from the tunica vaginalis or the connective tissue between the cremasteric fibers.

Diagnostic Aspiration.—Huhner⁷⁸ reiterated his advocacy of aspiration of the testis as a prognostic and diagnostic procedure in sterility. He expressed the belief that operation should not be undertaken for relief of obstructive sterility without first aspirating the testis, to ascertain whether or not spermatozoa are present.

75. Pearlman, S. J.: Malignancy in an Undescended Abdominal Testis with Torsion, *J. Urol.* 18:637, 1927.

76. Valdoni, P.: Sarcoma primitivo della vaginale de testicolo, *Policlinico* 34: 244, 1927.

77. Chwalla, Rudolf: Ein Fall von Fibrosarkom des Samenstranges, *Ztschr. f. urol. Chir.* 23:419, 1927.

78. Huhner, Max: Aspiration of the Testicle in the Diagnosis and Prognosis of Sterility, *J. Urol.* 19:31, 1928.

INDEX TO VOLUME 17

| | PAGE | | PAGE |
|---|---------------------|--|----------|
| Colon, submucous lipoma of..... | 627 | Fractures—Continued | |
| ulcer of, simple nonspecific..... | 355 | late end-results in ununited fracture of | |
| Cooper, H. S. F.: Cause of death in high | 918 | neck of femur treated by bone peg or | |
| obstruction..... | | reconstruction operation..... | 712 |
| Copher, G. H.: "Stream line" phenomena in | | of fifth metatarsal bone..... | 714 |
| portal vein and selective distribution of | | of first cervical vertebrae..... | 712 |
| portal blood in liver..... | 408 | of lower end of radius..... | 713 |
| Cox, D. M.: Wounds of heart; report of 2 | 484 | of os calcis, treatment by arthrodesis..... | 711 |
| cases..... | | operative treatment for..... | 713 |
| Coxa Vara: See Hip Joint | | phenomena after..... | 708 |
| Craniotomy, incisions without forceps..... | 472 | pair..... | 813 |
| Crawford, A. S.: Craniotomy incisions with- | | review of 2 thousand..... | 709 |
| out forceps..... | 472 | role of circulation in healing of..... | 707 |
| Culligan, J. L.: Multiple renal stones; prob- | | Gallagher, W. J.: Effects of injections of | 420 |
| lems in treatment of patients with this | | acid and trauma on jejunal transplants | |
| condition..... | 259 | Effect of injections of hydrochloric acid | 279 |
| Cutting, R. A.: Relative mechanical strength | | on gastric and duodenal mucosae..... | 613 |
| of enterostomies performed with and | | Gallbladder, ascariasis of..... | 324 |
| without clamps; an experimental study. 658 | | Gangrene, spontaneous..... | 696 |
| Cysto-adenoma, chronic mastitis, adenoma | | Ghormley, R. K.: Thirty-sixth report of | |
| of breast and..... | 535 | progress in orthopedic surgery..... | 521, 689 |
| Cystoscopy..... | 874 | Goiter, toxic, and mental disease; relief | |
| Dandy, W. E.: Arteriovenous aneurysm of | | psychoses in thyrotoxic patients by | |
| brain..... | 190 | thyroidectomy..... | 296 |
| Venous abnormalities and angiomas of | | Gout..... | 533 |
| brain..... | 715 | Granuloma, in urinary tract..... | 889 |
| Danforth, M. S.: Thirty-sixth report of | | Hand, repair of nerves and tendons of.... | 703 |
| progress in orthopedic surgery..... | 521, 689 | Hart, D.: Acute empyema; treatment by | |
| Davison, W. C.: Empyema in infants under | | continuous tidal irrigation and drain- | |
| 2 years of age..... | 676 | age dependent on normal and respira- | |
| DeCourcy, J. L.: Toxic goiter and mental | | tory movements..... | 102 |
| disease; relief of psychoses in thyrotoxic | | Hart, V. L.: Spontaneous dislocations of | |
| patients by thyroidectomy..... | 296 | hip joint during early life; report of | |
| Diabetes Mellitus, bone development in dia- | | 28 cases..... | 587 |
| betic children..... | 700 | Heart, wounds of, report of 2 cases..... | 484 |
| Diagnosis, urologic..... | 349 | Hematoma, perirenal..... | 172, 892 |
| Diaphragm, function of..... | 840 | Hexylresorcinol, solution S. T. 37 (liquor | |
| Diathroses: See Joints | | properties of..... | 834 |
| Dick, B. M.: "Stream line" phenomena in | | Hip joint, limps caused by diseases of.... | 701 |
| portal vein and selective distribution | | pathologic dislocation of..... | 714 |
| of portal blood in liver..... | 408 | spontaneous dislocations of, during early | |
| Drop Foot: See Foot | | life..... | 587 |
| Elbow, fractures of..... | 710 | treatment of coxa vara..... | 704 |
| tennis, treatment of..... | 703 | tuberculosis of, result of treatment..... | 691 |
| Embolism, fat..... | 179 | Horine, C. F.: Physiology of liver and in- | |
| Empyema, acute; treatment by continuous | | testine; method of study..... | 289 |
| tidal irrigation and drainage depen- | | Hydrocele..... | 1074 |
| dent upon normal respiratory move- | | Hydrochloric acid, effect of injections of, | |
| ments..... | 102 | on gastric and duodenal mucosae..... | 613 |
| Enterostomy: See Intestines | | effects of injections of, on jejunal trans- | |
| Epididymitis..... | 676 | plants to stomach..... | 279 |
| Epiphysitis, acute, pathogenesis and treat- | | Hydronephrosis..... | 173, 880 |
| ment of..... | 1077 | Hyperesthesia, surgical significance of ab- | |
| Epispadias..... | 694 | dominal reflexes..... | 854 |
| Fairchild, F. R.: Cancer of lower lip; sug- | | Intestines, anastomosis, biliary intestinal, | |
| gestions as to operative technic on plas- | | for obstructive jaundice; analysis of | |
| tic repair..... | 630 | 137 consecutive cases..... | 1 |
| Femur, fracture of internal condyle of.... | 713 | effects of acid injections and trauma on | |
| results in ununited fracture of neck of | | jejunal transplants to stomach..... | 279 |
| femur treated by bone peg or recon- | | effect of solutions of pituitary and various | |
| struction operation..... | 712 | drugs on movements of small intestine | |
| Fincher, E. F., Jr.: Intramedullary lipoma | | during simple mechanical obstruction.. | 996 |
| of spinal cord; complete operative re- | | enterostomies, relative mechanical strength | |
| mova..... | 829 | of, performed with and without | |
| Fistula of bladder..... | 1058 | clamps..... | 658 |
| Foot, fracture of fifth metatarsal bone.... | 714 | high obstruction, cause of death..... | 918 |
| operative correction of drop foot..... | 706 | intra-intestinal pressure in obstruction.. | 507 |
| results of stabilization of paralytic feet. | | obstruction, relation of bacillus welchii | |
| spontaneous recovery of deformity of, fol- | | antitoxin to toxemia of..... | 860 |
| lowing laminectomy for spina bifida | | physiology of liver and..... | 289 |
| occulta..... | 699 | strangulation obstruction; comparison of | |
| Foreign bodies, in bladder..... | 1062 | toxicity of intestine and other tissues | |
| in kidney..... | 166 | autolyzed in vivo and in vitro..... | 431 |
| Foulds, G. S.: Review of urologic surgery | | tuberculosis of, causing obstruction..... | 440 |
| Fractures, about the elbow..... | 161, 331, 872, 1051 | Jaundice, obstructive, biliary intestinal | |
| compound, of tibia..... | 710 | anastomosis for..... | 1 |
| compression, of spine..... | 713 | Joannides, M.: Surgery of lung; care of | |
| dislocation of shoulder..... | 711 | stump in pneumectomy and in lobec- | |
| industrial, disability and cost of..... | 475 | tomy..... | 91 |
| in Great Britain, influence of surgical | | | |
| experience during the great war on | | | |
| treatment of persons with..... | 708 | | |

Hydrocele.—Campbell⁷⁰ analyzed 502 cases of hydrocele observed at the Bellevue Hospital. He pointed out that hydrocele in infants is rare, practically always congenital and associated with hernia. Ninety per cent of the patients were more than 21 years of age; 27 per cent were between 20 and 30. The right side is slightly more often affected than the left. Bilateral hydrocele was noted in four cases. The shortest duration was three days, and the longest sixty years. In more than 50 per cent of cases, the duration was between two months and three years.

Inflammation in the form of epididymitis is probably the most frequent precursor of acute or chronic hydrocele. This is most frequently gonorrheal; it may be tuberculous, and at times nonspecific. Careful examination of the exposed epididymis will in most cases reveal a pathologic organ showing the postinflammatory changes of hypertrophy or atrophy. Occasionally, hydrocele follows or accompanies orchitis. One patient had mumps immediately preceding the appearance of the hydrocele. Trauma may be and not infrequently is an etiologic factor. Thirty-four patients of this series noted an actual blow to the testis preceding onset of swelling. Campbell pointed out that operative trauma in the region of the spermatic cord, such as herniotomy entails, may cause hydrocele, and warned against undue injury to the vaginalis and testis during such procedures. Congenital hydroceles in adults are rare since the condition, if present, usually disappears spontaneously in infancy. The majority fall into the idiopathic group, but Campbell believes that unrecognized asymptomatic epididymitis is again the usual underlying process.

Pathologically, the fluid of uninfected hydroceles resembles blood serum, has a specific gravity of 1.020 to 1.026, and contains fibrin, albumin, paraglobulin, and at times cholesterin and phosphatic calculi. Microscopically, endothelial cells, cholesterin crystals, leukocytes, often spermatozoa, bacteria in infected cases, and in the event of hemorrhage, erythrocytes are shown. Caforio is quoted as stating that in view of the lower specific gravity and smaller serum content of transudates, fluid in the hydrocele is an exudate of inflammatory origin.

Symptomatically, if hydrocele is acute and the result of inflammation of the epididymis or testis (rarely trauma), pain is likely to be severe. Pain is usually proportionate to tension, severe with rapidly forming hydrocele accompanying acute gonorrheal epididymitis, and slight or absent with hydrocele and tuberculous epididymitis. Chronic hydrocele, uncomplicated by infection, is usually without symptoms save for

⁷⁰ Campbell, M. F.: *Hydrocele of the Tunica Vaginalis: Study of 502 Cases*, *Surg. Gynec. Obst.* 45:192, 1927.

INDEX TO VOLUME 17

[illegible]

swelling. Some patients complain of a dragging sensation in the scrotum or along the cord due to the weight of the mass.

In cases of hydrocele of the tunica vaginalis, inspection reveals a pear-shaped tumor tapering into the cord. As a rule the outline is felt to be smooth and regular and the mass elastic. Occasionally, lobulation is noted. The mass is dull to percussion, transmits light, cannot be reduced (except the congenital type), and unless complicated by hernia, does not give impulse. The cord is normal unless involved in the hydrocele. The scrotal skin may be tense and shiny over acute hydroceles and over chronic large hydroceles. Usually, testitis occurs behind and below the center of the tumor; rarely is it anterior and often it cannot be localized. Although puncture and withdrawal of the fluid is the surest diagnostic procedure, it should never be used unless hernia can be ruled out absolutely.

In the differential diagnosis, hernia, spermatocele, hematocele, chylocele, gumma, edema of chronic passive congestion and testicular neoplasm are considered.

Tapping or the use of a local irritant, such as painting the overlying skin with tincture of iodine, frequently accomplishes cure in infants; sometimes cure is spontaneous. In adults, spontaneous cure is never obtained. Internal medication is of no value. Tapping with or without injection and open operation are employed now in treatment. Tapping is often curative in cases of children and may be used for adults if they refuse operation and for those whose physical condition does not warrant operation. Injection of from 5 to 20 minims (0.3 to 1.25 cc.) of pure phenol after completely emptying the sac, with kneading of the scrotum to disseminate the drug to all surfaces, may be employed in uncomplicated hydroceles with thin walls and clear fluid. It should not be employed for children if it cannot be determined whether or not the sac communicates with the abdominal cavity; if it does, fluid will reform.

Open operation is the treatment of choice. Simple eversion (the bottle operation of Andrew) is useful for small hydroceles without thickened sacs. Volkmann incised the sac widely and swabbed the cavity with phenol. Convalescence is slow and the percentage of recurrences high. Campbell prefers the excision and eversion operation of Winkelman. Cutaneous and deep injections of procaine for anesthesia are made, the cord is isolated and thoroughly infiltrated, thus affording complete testicular block. By carefully incising the parietal tunica until the innermost layer presents a bluish hue, much hemorrhage may be prevented in later dissection. If the hydrocele is unusually large, most of the fluid is withdrawn before the sac is incised. With hydroceles of ordinary size, the practice is to mobilize the unopened sac by blunt

INDEX TO VOLUME 17

| | PAGE | | PAGE |
|--|---------------------|--|---------------------|
| Rienhoff, W. F., Jr.: Empyema in infants under 2 years of age..... | 676 | Tuberculosis—Continued | |
| Robinson, W. H.: Role of circulation in healing of fractures..... | 420 | intestinal, causing obstruction..... | 440 |
| Roentgen rays, examination of urinary tract | 891 | of bladder | 1061 |
| | | of hip, results of treatment..... | 691 |
| Sachs, E.: Intramedullary lipoma of spinal cord; complete operative removal..... | 829 | of kidney | 166, 885 |
| Sarcoma, chronic ulcerative colitis associated with malignant disease..... | 561 | of knee, in adults..... | 692 |
| malignant tumors of chest wall..... | 459 | of prostate | 1071 |
| Scholl, A. J.: Review of urologic surgery..... | 161, 331, 872, 1051 | rice bodies in..... | 693 |
| Scoliosis | 526 | synovial | 694 |
| sciatic, etiologic factors in..... | 528 | urogenital | 1078 |
| Shoulder, dropped, operation for slinging..... | 703 | Tumors: See also Cancer; Lipoma; Myeloma; Sarcoma | |
| fracture dislocation of..... | 475 | arteriovenous aneurysm of brain..... | 190 |
| pain in | 702 | epithelial neoplasms of peripheral and cranial nerves | 117 |
| pressure on brachial plexus by normal first rib | 529 | malignant, of chest wall..... | 459 |
| Smith-Peterson, M. N.: Thirty-sixth report of progress in orthopedic surgery..... | 521, 689 | of bladder | 345, 1051 |
| Spinal cord, intramedullary lipoma of; complete operative removal..... | 829 | of brain | 715 |
| tumors of cauda equina and..... | 691 | of cauda equina and spinal cord..... | 691 |
| Spine, abdominal symptoms and chronic strain of | 527 | of cervical spine | 690 |
| cervical, tumors of..... | 690 | of tendon sheaths | 689 |
| compression fractures of..... | 711 | of testis | 348, 1072 |
| fractures of first cervical vertebrae..... | 712 | renal | 886 |
| lumbar, abnormalities of..... | 528 | suprarenal | 893 |
| surgery: See Laminectomy | | synoviatonia | 689 |
| tuberculosis, comparative results of operative and nonoperative treatment of Pott's disease in children..... | 692 | Ulcer: See also Peptic Ulcer | |
| Stabins, S. J.: Relation of bacillus welchii antitoxin to toxemia of intestinal obstruction; experimental studies..... | 860 | simple, nonspecific, of colon..... | 355 |
| Stomach, effects of acid injections and trauma on jejunal transplants to..... | 279 | Ureter, carcinoma of..... | 897 |
| effect of injections of hydrochloric acid on gastric and duodenal mucosae..... | 613 | diverticula | 898 |
| Stone, H. B.: Intra-intestinal pressure in obstruction | 507 | stone | 896 |
| Suprarenals, tumors of..... | 893 | transplantation | 331 |
| Syphilis, of bladder | 1062 | trauma of | 898 |
| | | ureteral activity in some pathologic conditions; studied by graphic manometric method | 968 |
| Taylor, R. T.: Fracture dislocation of shoulder; relation of soft parts to restoration; new method of treatment..... | 475 | Urethra | 349 |
| Tendons, of hand, repair of..... | 703 | tumors of | 1079 |
| spontaneous dislocation and destruction of tendon of long head of biceps brachii; 59 instances..... | 493 | urethrography | 872 |
| tumors of tendon sheaths..... | 689 | Urinary Tract, roentgen-ray examination of | 891 |
| Testicles, diagnostic aspiration..... | 1074 | Urologic surgery, review of..... | 161, 331, 872, 1051 |
| infarction of testis..... | 348 | Urology, urologic diagnosis..... | 349 |
| torsion of testis..... | 347 | | |
| tumors of | 1072 | Varicocele | 1077 |
| Theis, F. V.: Ligation of artery and concomitant vein in operations on large blood vessels | 244 | Veins, arteriovenous aneurysm of brain..... | 190 |
| Thompson, H. L.: Exstrophy of bladder complicated by carcinoma..... | 641 | ligation of artery and concomitant vein in operations on large blood-vessels..... | 245 |
| Thorax, malignant tumors of wall of chest..... | 459 | portal, "stream line" phenomena in portal vein and selective distribution of portal blood in liver..... | 408 |
| Thyroidectomy, relief of psychoses in thyrotoxic patients by..... | 296 | Verbrugge, J.: Review of urologic surgery..... | 161, 331, 872, 1051 |
| Tibia, old infected compound fractures of; premature ossification of lower epiphysis of, following forcible correction of clubfeet | 521 | Vital Capacity, its significance in relation to postoperative pulmonary complications | 304 |
| Toxemia, of intestinal obstruction, relation of bacillus welchii antitoxin to..... | 860 | | |
| Toxin and antitoxin, relation of bacillus welchii antitoxin to toxemia of intestinal obstruction | 860 | Waldron, G. W.: Studies in intestinal obstruction; strangulation obstruction; comparison of toxicity of intestine and other tissues autolyzed in vivo and vitro | 430 |
| Trattner, H. R.: Ureteral activity in some pathologic conditions; studied by graphic manometric method..... | 968 | Wangansteen, O. H.: Studies in intestinal obstruction; strangulation obstruction; comparison of toxicity of intestine and other tissues autolyzed in vivo and vitro | 430 |
| Trauma, as factor in acute appendicitis..... | 672 | Watt, J. C.: Development of bone; (a) process of development in bones of different types; (b) normal physiologic calcification of matrix in cartilage and in bone; (c) problem of manner of deposition of calcium salts..... | 1074 |
| Tuberculin, quantitative reaction of..... | 693 | Weinberg, J. A.: Intra-intestinal pressure in obstruction | 507 |
| Tuberculosis, comparative results of operative and nonoperative treatment of Pott's disease in children..... | 692 | Weintrob, M.: Blood supply to appendix..... | 577 |
| experimental, effect of rachitogenic diet on | 693 | Wilder, R. M.: Oxygen in treatment of postoperative bronchopneumonia..... | 1047 |
| | | Wilson, P. D.: Thirty-sixth report of progress in orthopedic surgery..... | 521, 689 |
| | | Wolfer, J. A.: Pancreatic function tests; with special reference to quantitative determination of fecal amylase..... | 899 |
| | | Wounds, of heart; report of 2 cases..... | 484 |
| | | Wright, I. S. Bactericidal properties of solution S. T. 37 (liquor hexylresorcinolis 1:1,000) | 834 |
| | | Wrist, fractures of lower end of radius... | 711 |

The more unfavorable complication has been for the pus to reach the subcutaneous tissues and to dissect beneath the skin, at times causing an infection more serious than the empyema, and necessitating multiple incisions; occasionally, if not recognized early, it has led to a fatal termination. This danger is greatest when the hemolytic streptococcus is the organism that causes the empyema.

In the class of minor disadvantages may be placed the presence of thick pus, which makes the irrigation of the cavity slow and difficult; the tendency, as healing progresses, to overdilate the cavity which is tending to collapse; the leakage of pus around the tube, demanding frequent dressings; and the plugging of the tube, causing almost continuous irritation and annoyance to every one concerned in the care of the patient.

In considering various methods to overcome these difficulties, it was thought that the natural movements of the chest with their pumping action could be utilized to give a continuous irrigation, and at the same time avoid the possibility of forcing in fluid under pressure. The original plan was to use an inflow and an outflow tube, each equipped with valves. It was found, however, that a simple tidal flow through as short a tube as possible was entirely satisfactory and gave the least possibility of becoming obstructed. With a continuous flow in one direction, fibrin blocks the opening to the outlet tube, but with the tidal flow it becomes dislodged at the next inspiration when the fluid flows into the chest.

The irrigation apparatus shown in figure 1 was soon adopted. This consists of a rubber tube which is passed into the dependent part of the empyema cavity through a trocar thoracotomy wound, and just outside the chest is connected by means of a T tube with a rubber bag on one side and on the other with a rubber tube leading through a Y tube to an irrigation bottle above and a drainage bottle below. The rubber bag is strapped to the abdomen just below the trocar thoracotomy wound, placing it slightly below the level of the empyema cavity with the patient in Fowler's position. This gives a slight amount of suction at all times. Since the entire system is closed, it is impossible for air to enter if fluid is kept in the irrigation flask and the drainage tube is always, when unclamped, below the level of the solution in the drainage bottle. This statement presupposes that the empyema is not complicated by a bronchial fistula, and that the tube fits snugly within the opening through the wall of the chest. The bag can be entirely emptied and suction applied to the empyema cavity by removal of the clamp to the drainage bottle. When this condition has been maintained for the desired length of time and the bag is partially refilled, there is no possibility of causing a positive pressure within the empyema cavity. The bag is never completely distended and usually is only from one-fourth to one-half full.

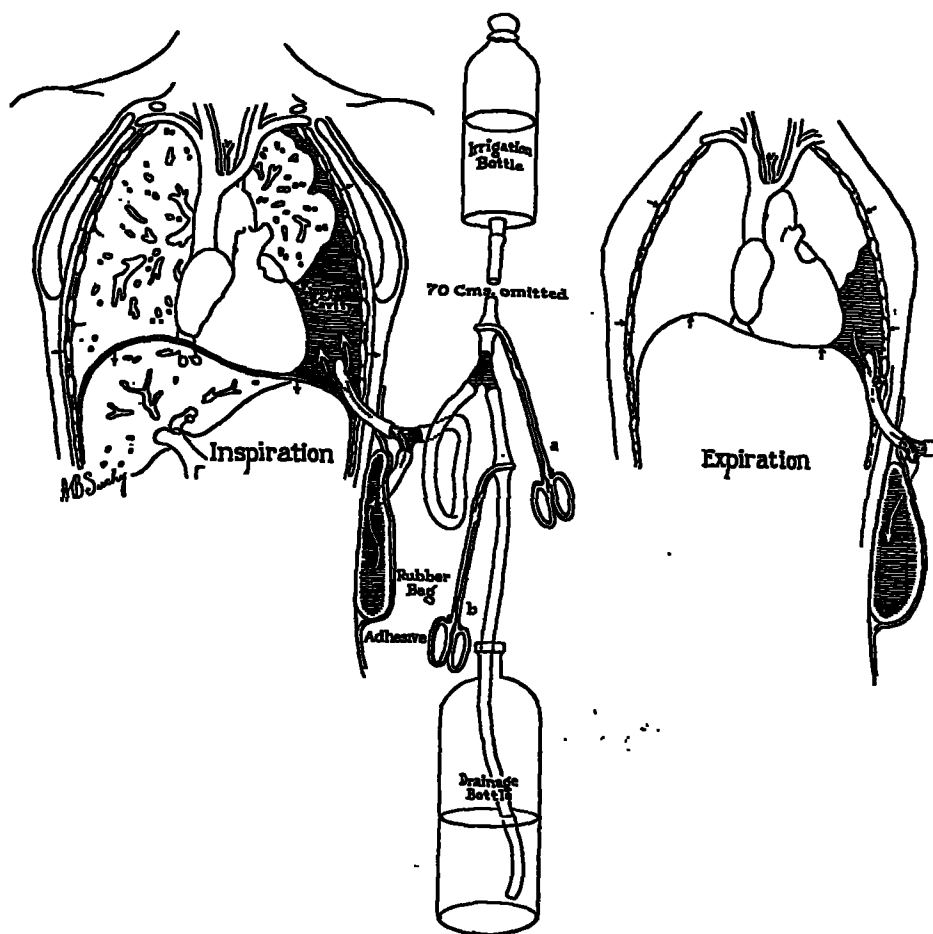


Fig. 1.—Diagrammatic illustration of the apparatus connected with the empyema cavity as shown in a cross-section of the chest. On the left is illustrated the effect of inspiration with enlargement of the thoracic cavity, and the reduction of the intrathoracic pressure below the surrounding atmospheric pressure. Thus the atmospheric pressure forces the fluid within the rubber bag strapped to the abdomen into the empyema cavity. With expiration, illustrated on the right, the intrathoracic space is passively or forcibly compressed with the outflow of air from the lungs and also of fluid from the empyema cavity, resulting in a diminution in the size of the cavity. This continues with each respiration, the consistency of the fluid within the empyema cavity and the rubber bag gradually approaching a common level. Before this is reached, however, clamp *b* is removed, the rubber bag is completely emptied, as much fluid as possible is siphoned from the empyema cavity, clamp *b* is reapplied, and clamp *a* is removed until the desired quantity of clean solution has flowed into the rubber bag and empyema cavity. The gradual mixing by means of the tidal flow again begins, and thus the consistency of the fluid within the empyema cavity gradually approaches that of the irrigating solution, the final point of dilution being determined by the amount of irrigation fluid kept in the bag, the frequency of its replacement, and the division of the time between irrigation and suction.

cavity, and with the patient in Fowler's position, there is always a slight amount of suction, but not enough to prevent a free tidal flow.

For the most efficient interchange of fluid by the tidal flow, the amount of tubing between the empyema cavity and the rubber bag is cut to the minimum.

Numerous types of rubber bags have been tried, such as the Vorhees bag, blood pressure cuff, mouth piece for a gas anesthesia machine, and others. It is desirable, however, to have a bag with the tube entering it about the middle of the longitudinal axis; a football bladder best meets this requirement. There are two distinct advantages in this type of bag:



Fig. 3.—Close view of the apparatus shown in figure 2, and with the short tube strapped in the chest with adhesive; the tube to the football bladder, which had just replaced an old blood pressure cuff, was later shortened. The lower end of the bladder is turned in to diminish its size. The only care which this case demanded was observation for the proper distribution of the time between irrigation and suction, and renewal of the adhesive dressings about once every two weeks.

The first advantage is that all particles of fibrin and coagulated pus will settle to the dependent point away from the opening of the tube, so that when they enter the bag they are trapped. Incidentally, the tube in the chest entering at the dependent part of the empyema cavity tends to remove the thicker material as it settles out. The second advantage comes into play late in the treatment, after the tube in the chest becomes a little loose. At that time any air which may enter the irrigation system rises to the top and is trapped as soon as it is forced into the bag. The

The frequency with which the fluid should be renewed within the bag depends on the individual case. Early in the treatment, or when the cavity is large, it is renewed every hour in order to keep the pus relatively thin, while later, when the cavity is small and clean, the bag can be refilled only a few times within the twenty-four hours. This avoids disturbing the patient at night, but at the same time gives him the advantage of continuous irrigation.

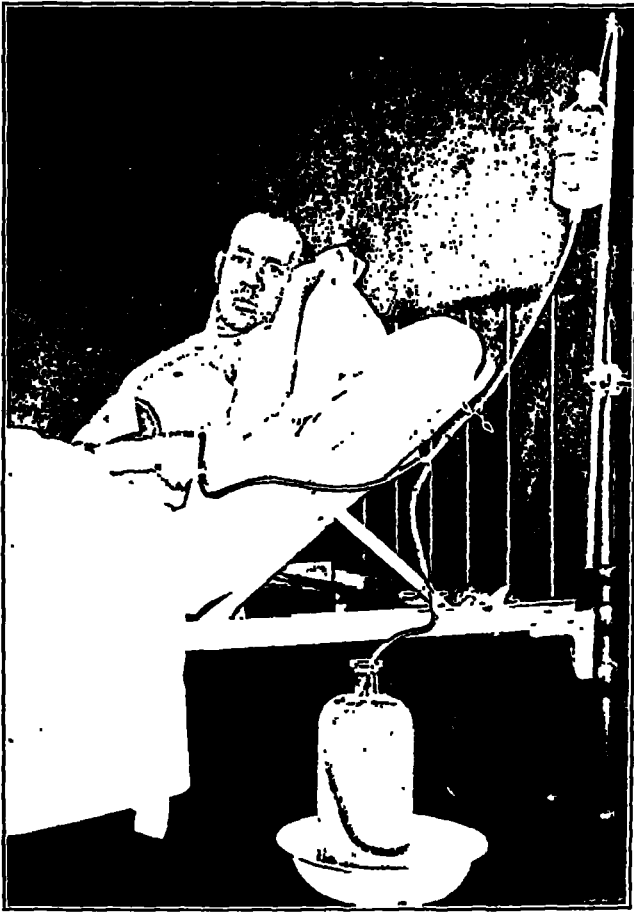


Fig. 2.—Irrigation apparatus in use. This photograph was taken after six weeks of treatment, the patient having a massive hemothorax with infection (figs. 3, 4, and 5). Not once during this time did the tube become plugged; the adhesive holding the tube in place was not changed during the first month, and the apparatus was out of order on only one occasion when the patient, while delirious, left his bed and pulled the irrigation bottle from its stand.

The proportion of time given over to suction and to irrigation depends entirely on the amount and rate of formation of pus. My plan has been to run the irrigation as much of the time as is necessary to keep the cavity clean and the contained fluid thin and relatively clear. The remainder of the time is given over to suction by the siphon. With the bag strapped to the body a little below the level of the empyema

who have gone for from four to seven weeks without having the original tube removed or plugged at any time. One patient (figs. 2 and 3) went for a month without having the adhesive and small dressing about the tube removed, and at no time was there plugging of the tube or any cessation in the tidal flow of the fluid. Consequently, there was at no time any positive pressure of sufficient degree to force fluid out around the tube; also there was no suction of air as the tube fitted

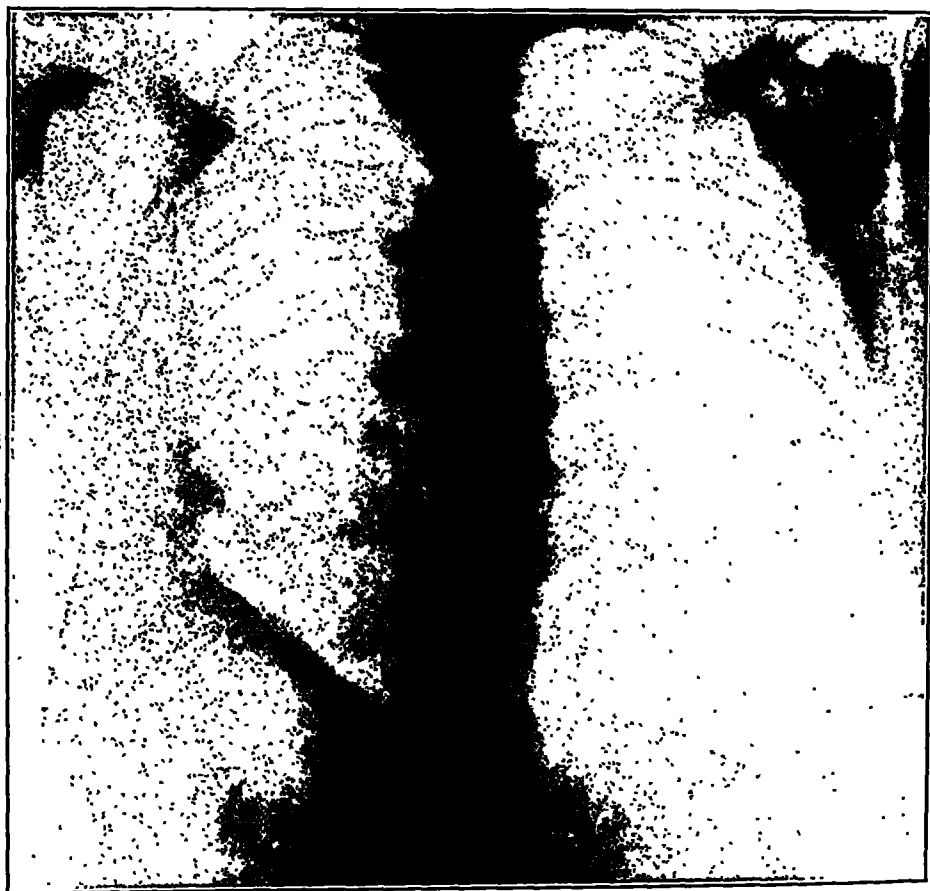


Fig. 5.—Same patient as figure 4, after ten weeks of treatment with continuous irrigation of, or suction on, the empyema cavity. The cavity had completely closed, and the temperature, which had been from 101 to 104 F. before operation, was below 100 F. after the fourth postoperative day. Note the high position of the diaphragm on the left side, its sharp rise from the midline outward until it fuses with the strip of thickened pleura. Below this point it is apparently adherent to the wall of the chest, thus helping to obliterate the empyema cavity after the long collapse of the lung.

The treatment in subsequent cases leads us to believe that the postoperative course here could have been shortened by giving more time to suction, by the earlier institution of forced expiration against an obstacle, with the lungs filled with air, and by inserting the tube through the chest at a lower level.

snugly. At the end of this time, the granulating sinus was free from excessive infection. Another patient went for eight weeks without

thick pus and the air are removed when the fluid within the bag is replenished with fresh solution. Any bubbles of air in the tube to the irrigation bottle are likewise forced into the bag and trapped in its upper part when it is refilled with fresh irrigating fluid.

In the application of this apparatus, the fluid cannot be forced into the chest as long as the rubber bag is not more than from two-thirds to three-fourths full, and frequently it is kept only from one-third to one-fourth full. For children, the lower end of the bag is sometimes

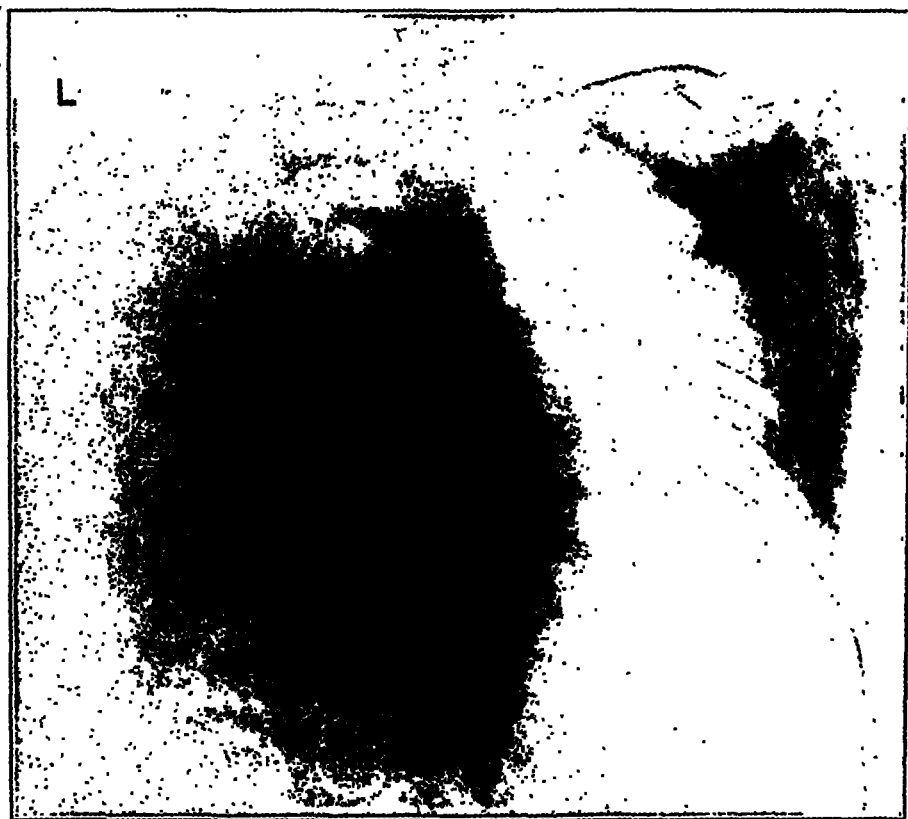


Fig. 4.—An enormous, infected left hemothorax following a stab wound of the chest. Over a period of two months repeated efforts were made to aspirate the fluid, but without result. The collection of fluid increased in size and there was a progressive rise of temperature until the clot became sufficiently fluid to aspirate. The fluid promptly reformed, the cultures were positive for *Streptococcus viridans*, and a trocar thoracotomy was performed.

turned in, as in figures 2 and 3, the size thus being decreased. This absence of positive pressure prevents the forcing of infected material out around the tube, particularly when the cavity has closed down until it holds only a few cubic centimeters, less than the amount of the tidal flow in the beginning of the treatment, and when one's tendency is to run in more solution than the cavity will hold.

The continuous movement of the fluid prevents any coagulation of fibrin and blocking of the tube. This has been proved by several patients

tidal irrigation of the empyema cavity where the apparatus is in use. The blowing is also most efficient when this apparatus is applied, for there is absolutely free egress of fluid when pressure is made on the cavity by the forced expiration. Suction can be applied as desired to hold the lung in the position of expansion or to aid in the expansion obtained by forced expiration with the lungs full of air.



Fig. 7.—Same chest as shown in figure 6, after twenty-four days of treatment by continuous tidal irrigation and suction. The patient was ill, and following operation there was a sharp rise of temperature to 104 F., with a drop to 100 F. the following morning. There was immediate and constant improvement, the patient's temperature remaining around 99 F. to 100 F., with a few elevations explainable by severe abscesses over the back. At the time this picture was taken the cavity holds less than 8 cc., and a rapid healing is anticipated.

With this opening freely patent at all times, and with the continuous irrigation, the drainage must be as good as, if not better than, with a rib resection and a larger opening.

cavity not surrounded by dense scar tissue. With the tube to the drainage bottle open, there was still considerable pressure within the rubber bag, and this could not be relieved until the drainage tube was emptied of fluid and its lower end raised above the level of the fluid in the drainage bottle.

To overcome this complication, the apparatus illustrated in figure 10 was devised. This consists of a flask partially filled with irrigating fluid, connected by an opening at its dependent part to a short tube entering the empyema cavity. An irrigation bottle is connected to an opening at the top of the flask, while through a cork is passed a tube opening to



Fig. 9.—Same chest as in figure 8 after forty-eight hours of treatment with continuous tidal irrigation. The pus was thick, but the tidal flow was perfectly satisfactory for the first fifteen hours.

Apparently at that time the lung had expanded sufficiently to permit of the two pleural surfaces rubbing together with the respiratory movements, and the shaggy exudate over the surface was dislodged. As soon as this was removed from the empyema cavity by manipulating the tube and by frequent irrigations, there was no further embarrassment to the free flow of the tidal irrigation, and there have been no other large masses of fibrin.

In the early morning at the time of the freeing of the large amount of fibrin and exudate, the patient's temperature was 104 F. However, forty-eight hours after the thoracotomy was performed, the temperature remained below 100 F. for the entire day.

As far as could be determined at that time, there was only a small amount of fluid within the empyema cavity.

Not the least of the advantages is the interest which the patient manifests in the irrigation. This applies equally to the child, who is proud of the apparatus and treats it like a toy, watching the motion of the fluid and the particles of pus darting back and forth, and to the adult, who on seeing flakes of fibrin in the tube moving with the tidal flow, will deliberately, with a long and forced expiration, force them into the bag, where they settle down to the bottom and are eventually siphoned off to the drainage bottle.



Fig. 8.—Chest of a boy, aged 5, with a pneumococcus, type IV, empyema. The history suggested the onset with pneumonia for a week, followed by the empyema, which had been present for five weeks. Over this period there had been pain in the chest, high fever, sweats, and a progressively downhill course.

ACUTE EMPYEMA COMPLICATED BY BRONCHIAL FISTULA

In cases of acute empyema with a bronchial fistula in which the patient did not cough up the pus from the cavity, irrigation was tried. If, as frequently happened, this did not produce irritation and coughing, the irrigation apparatus shown in figures 1, 2 and 3 was used. This proved to be unsatisfactory, however, since the continual leakage of air into the empyema cavity soon filled the rubber bag with air until it was under marked pressure. There must of necessity have been some associated compression of the lung where the empyema was acute and the

harm comes from the entrance of air into the chest, since it is continually coming in through the bronchial fistula, while if the siphoning action is destroyed by air entering the tube, it is readily reestablished by closing clamp *c*, clamping off the tube to the empyema cavity, and opening clamps *a* and *b*. Suction can be applied as desired by closing clamp *c* with the flask relatively full, and opening the siphon on a closed cavity by removal of clamp *b*. By this means it can be determined when the fistula is closed, suction can be used as desired, and after it is proved



Fig. 11.—Chest of a girl, aged 5, with an acute pyopneumothorax of unknown duration, just before a trocar thoracotomy was performed. A bronchial fistula was present, and the cavity was treated by continuous tidal irrigation, using the apparatus shown in figure 10. The temperature dropped to normal and remained below 100 F. for the postoperative course.

that there is no further leak, the case can be treated like a simple empyema.

This apparatus is to a certain extent cumbersome, and demands rather careful adjustment; the flask cannot be completely emptied, and the opening to the chest is near the bottom of the flask where the thicker pus collects. However, it has proved satisfactory in the cases in which it was used. It seems likely that it will be desirable to replace it by a rubber bag, which provides for the ready escape of the air which enters from the bronchial fistula.

There is only late and negligible leakage around the tube in the thoracotomy wound, so that dissecting infections do not occur, and dressings are practically eliminated.

Suction can be applied as desired, even as long as from six to eight weeks after operation, when expansion of the lung is slow after long compression. Even then there is little if any leakage of air around the tube in the thoracotomy wound.

The apparatus used in the presence of a bronchial fistula permits the immediate escape of air from the drainage system without the possibility of the air reentering the chest or disturbing the siphoning action.

By this method of treatment, the closing of the empyema cavity is more rapid than by the early institution of rib resection and open drainage.

With the use of the flask there is the least limitation to the movements of the patient and the minimal traction on the tube entering the chest; and every possibility of spilling the irrigation solution in bed is avoided by suspending the flask from an overhead frame so that it just clears the bed and normally hangs immediately adjacent to the thoracotomy opening.

SUMMARY

A method is described with illustrations of the apparatus used in treating patients who have acute empyema, with or without the compli-

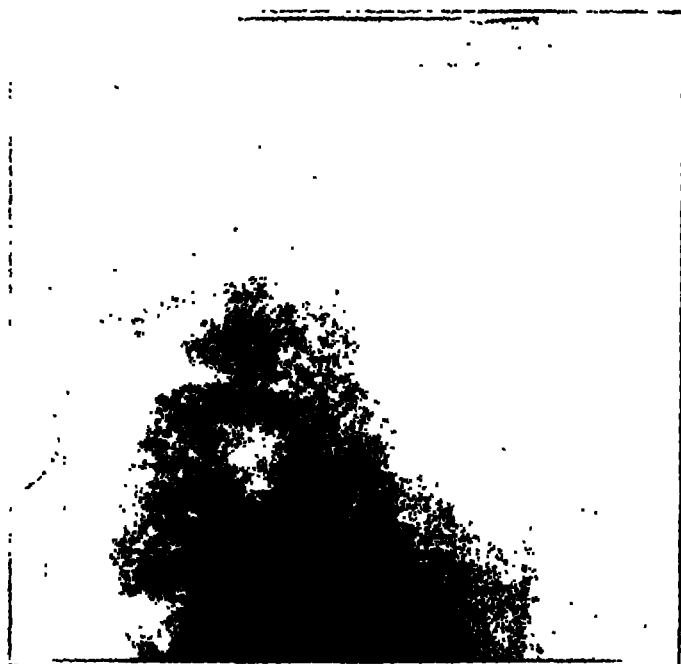


Fig. 12.—Same chest as figure 11, taken on the thirteenth postoperative day. At this time the tidal irrigation system ceased to work, and on attempting to open the tube it was found that there was no cavity, but only a sinus the size of the rubber tube. The patient is apparently well, free from pain, and playing, with a normal temperature and practically no drainage from the sinus.

cation of a bronchial fistula, by continuous tidal irrigation carried on by the normal respiratory movements.

The trocar thoracotomy subjects the patient to the minimal operative procedure.

As the irrigation tube practically never becomes plugged, there is no obstruction to free drainage. In addition, the cavity is being continually washed out by relatively clean solution, so that there is more efficient cleansing and drainage than with the rib resection and open thoracotomy.

There is not the large raw surface to become infected by the continual soiling at the time of and following operation.

Operation.—June 12, 1922: The operation was performed by me with Drs. Woodruff and Lutterloh assisting. Ether anesthesia was given by Dr. Allgeyer. A preanesthetic hypodermic injection of one-fourth grain (0.016 Gm.) of morphine and one one hundred and fiftieth grain (0.0019 Gm.) of atropine was given. The anesthetic was started at 10:47 a. m., and discontinued at 12:06. The operation was started at 11 and was discontinued at 12:12, the procedure consisting of excision of the neuroma and transplantation of the median nerve into the ulnar nerve in the right arm.

An incision about $3\frac{1}{2}$ inches (8.87 cm.) long was made on the inner side of the biceps muscle corresponding to the course of the brachial artery. As soon as the soft tissue was dissected away and the muscles retracted, the large mass with the blood vessels came into view. The median nerve was isolated above the level of the tumor and a pair of forceps insinuated between the brachial artery and the median nerve to act as a support. After this the dissection of the tumor, which was continuous with the median nerve, was carried on, and the mass entirely separated from the brachial artery. It was shown to be a spindle-shaped mass about $2\frac{1}{2}$ inches (6.27 cm.) in its long axis and $\frac{3}{4}$ inch (1.9 cm.) transversely. In one place on the outer aspect of the mass, it had broken through as

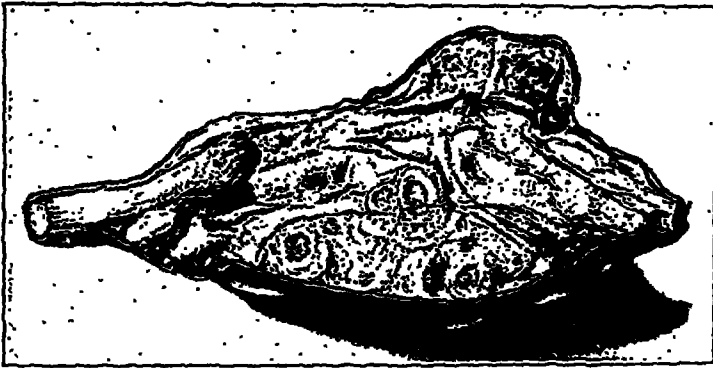


Fig. 1 (case 1).—Gross specimen of tumor of median nerve.

though there had been a slight hemorrhage. The lower limit of the tumor was just above the bicipital fascia (fig. 1).

Procaine hydrochloride was injected into the median nerve above the level of the neuroma, and a section was made of the nerve above. Then the nerve was sectioned below. This left a distinct gap of about $3\frac{1}{2}$ inches. It was impossible to consider elongation of the nerve to close the defect, and therefore the question of where to graft the distal end was considered. It was decided to utilize the ulnar nerve. This was exposed behind the internal condyle and isolated and mobilized. A tunnel was made under the pronator teres with a pair of forceps. The distal end of the median nerve was brought under the tunnel and grafted into the lateral aspect of the ulna with fine silk. The proximal end of the nerve, which was cut instead of being left unattached, was sutured to the internal cutaneous nerve, which was exposed in the wound. The wound was sutured in tiers with fine catgut to approximate the muscle and subcutaneous tissue. Michel's clips were used for the skin. Cross-section of the tumor showed that it contained a good deal of connective tissue and some degenerating areas which looked like colloidal material. A diagnosis of neuromyxosarcoma was made.

Laboratory examination showed a somewhat cylindric-shaped structure measuring 7 cm. in length and 3 cm. at its broadest diameter. It tapered at each

structure-like material. They were lined with cells that were tall and columnar in their general appearance, which were closely packed together, and on close study showed practically no separation of the individual cells; the appearance was that of a multinucleated syncytial mass resting on an underlying structure resembling a basement membrane. The entire glandular structure was divided into areas of various sizes by a cellular supportive material showing nuclei occupying a relatively large proportion of the cell; there was a minimum amount of intercellular substance. Most of the supportive structure was suggestive of nerve tissue, but I was unable to find positive evidence of a former nerve trunk anywhere except on the periphery. Mitotic figures were noted both in the epithelial and supportive cells. The blood supply of the part was not prominent, the vessels being present in stroma. A few areas of necrosis and degeneration were noted, but these were confined largely to the glandlike spaces. In some places, the stroma was myxomatous, and in others, it was made up of a denser tissue.



Fig. 3 (case 1).—High power magnification of first recurrence showing glandular elements.

A tentative diagnosis of carcinoma of the gland cell type was made, with the explanation that further study was required to determine definitely the primary origin (Lanford).

Progress Notes.—Following the operation, the patient had a sensation of pain and touch in the thumb and all fingers. He was able to flex and extend his wrist. Three days after operation, common sensation was noted in the peripheral distribution of the median nerve. The wound healed by primary intention. When the patient left the hospital ten days after the operation, common sensation was present as already noted.

During October, 1922, the patient returned, because a painful lump had developed in the upper portion of the wound caused by the previous operation. This was believed to be neuroma of the stump of the median nerve, and operation was advised.

Progress Notes.—On June 23, 1923, the patient returned because of the development of a mass on the inner aspect of the elbow. Examination at this time revealed the following: The patient was well developed and did not show any evidence of emaciation. With the exception of the tumor mass at the elbow, nothing in his condition indicated general discomfort. The scar of the previous operation on the right arm was healthy. The elbow was flexed at a right angle. There was little mobility of the joint, and the forearm was midway between pronation and supination. Some atrophy of the muscles of the hand was present, but sensation of pain, touch and temperature in the forearm was undisturbed. However, there was some diminution of sensation in the index finger.

Dr. Holbrook, a neurologist, examined the patient and reported: "Sensation of pin and cotton is good over the palmar surface of the right hand, except in

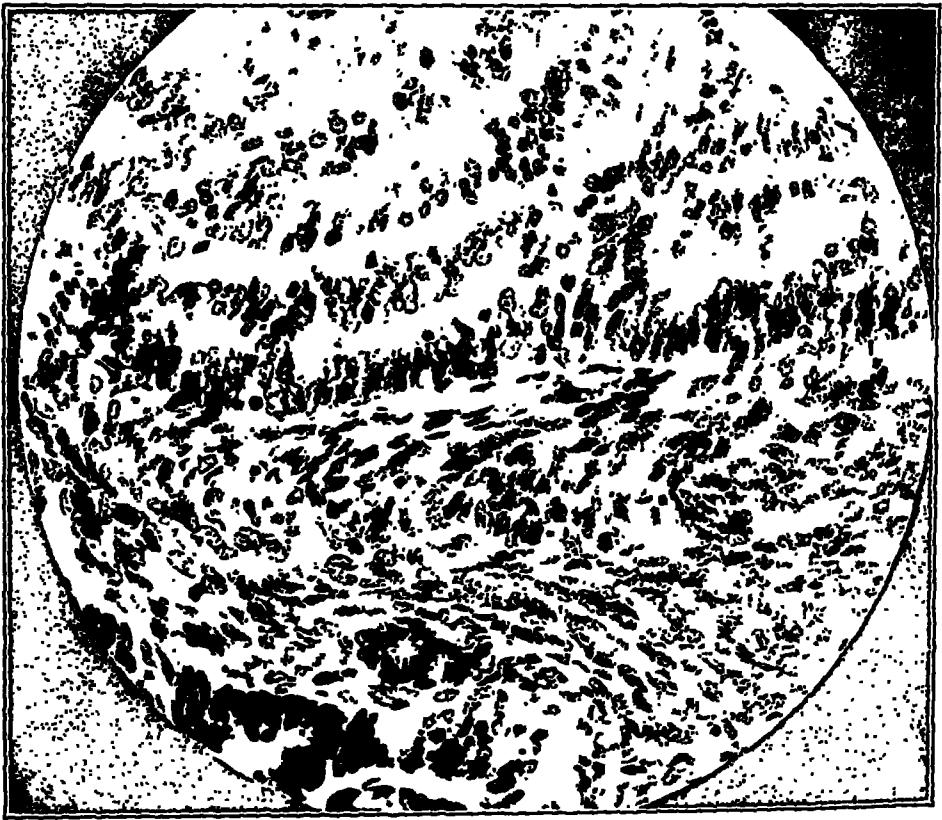


Fig. 5 (case 1).—High power magnification of first recurrence.

the index finger, in which sensation is dulled about the middle and beyond this point is absent. Thermal sensation is inaccurate over most of the hand, especially toward the index finger. Temperature differences are appreciated toward the center and inner side of the hand."

Third Operation.—On Jan. 25, 1923, I performed an operation with Drs. Macheca and Liles assisting. Dr. Allgeyer gave the ether anesthesia.

The amputation was made at the junction of the middle and upper thirds of the right arm. A tourniquet was applied, a circular skin flap dissected up, and the muscle cut at the level of skin retraction. The muscles were retracted and the humerus sawed through. The large nerves were then brought down into the field, and an inverted V-shaped excision of the end approximated the sheaths

median nerve at its anastomosis with the ulna. The belly of the flexor sublimis digitorum was ballooned out by the growth and gave the appearance of a funnel. In order to disturb the appearance as little as possible, Dr. Lanford took a small block of the tumor out of the ballooned portion of the palmaris longus belly. This was then sutured in order to retain the contour of the original growth.

Laboratory examination showed a specimen made up of the forearm and hand and about 6 inches (15.24 cm.) of the arm, which presented a tumor involving the structures at the bend of the elbow. In gross, the hand showed considerable atrophy changes, but otherwise was normal. A marked swelling was noted mostly at the bend of the elbow on the anterior surface, extending backward and laterally to involve most of the structures. The overlying skin was intact and loose over the growth, and there was a long, well healed scar from a former

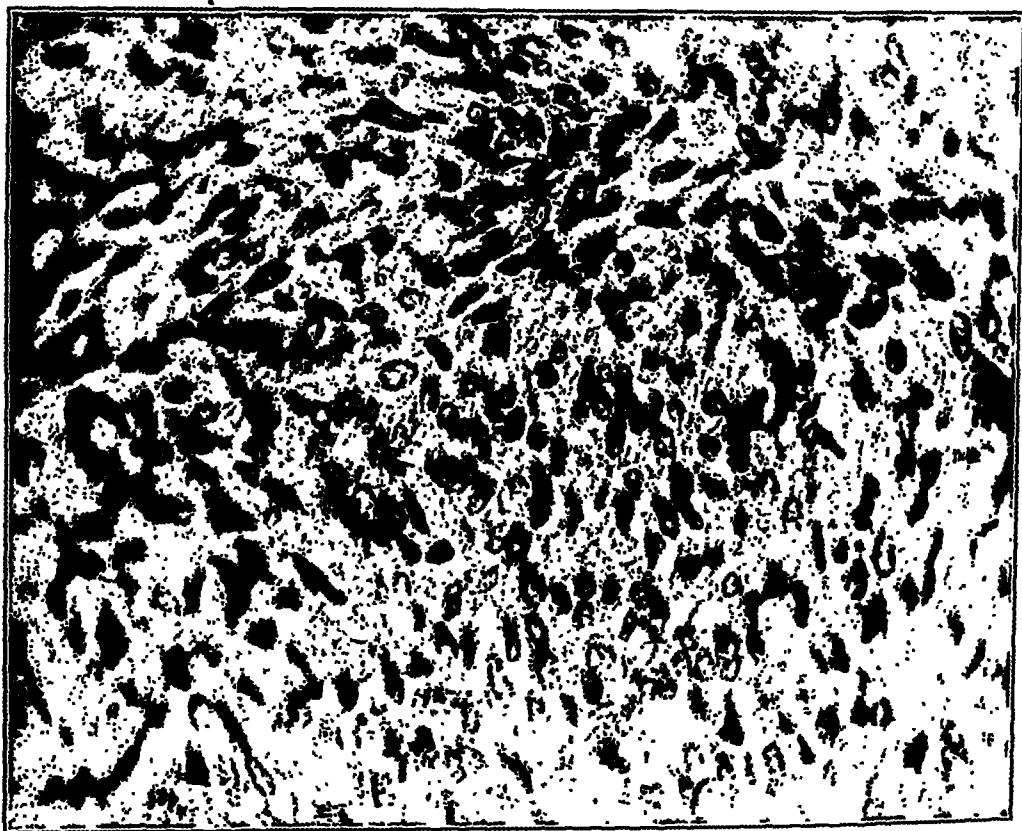


Fig. 7 (case 1).—High power magnification of second recurrence.

operative procedure. When the skin was dissected back, a new growth was found that had involved the muscles of the part, particularly all those inserted into the internal condyle of the humerus, and to a lesser degree those of the external condyle. The muscles were pushed upward and were thinned out, this being particularly noticeable in the superficial layer, while the deeper layer was more infiltrated and replaced by the main growth. The main mass was 11 cm. in length and 8 cm. at its thickest portion: it was roughly cylindric or funnel-shaped, the upper portion being at the bend of the elbow, and the pointed end extending onto the forearm. It was firm, and here and there presented nodulations which were smooth and were firmly adherent to the overlying muscle. On sectioning, it offered considerable resistance to the knife and presented a cut surface that was

with plain catgut, making a fish-tail appearance after the suggestion of Corner. The nerves were injected with 95 per cent alcohol following the suggestion of Carl Hoover and Lewis. The muscles were quilted over with plain catgut after ligation of the large vessels. Chromic catgut no. 2 was used for ligation. There was little bleeding. Interrupted plain catgut sutures were introduced into the sheath to diminish the amount of dead space. The skin was closed with silkworm and plain catgut interrupted sutures. The specimen was sent to the laboratory for preservation. Amputation was done because the removal of sufficient tissue to remove the entire mass would leave a useless arm.

A gross specimen was taken from an amputation of the lower third of the arm and forearm. The dissection was done by Dr. Lanford, and the line of the previous incision along the course of the ulnar nerve was incised. The skin

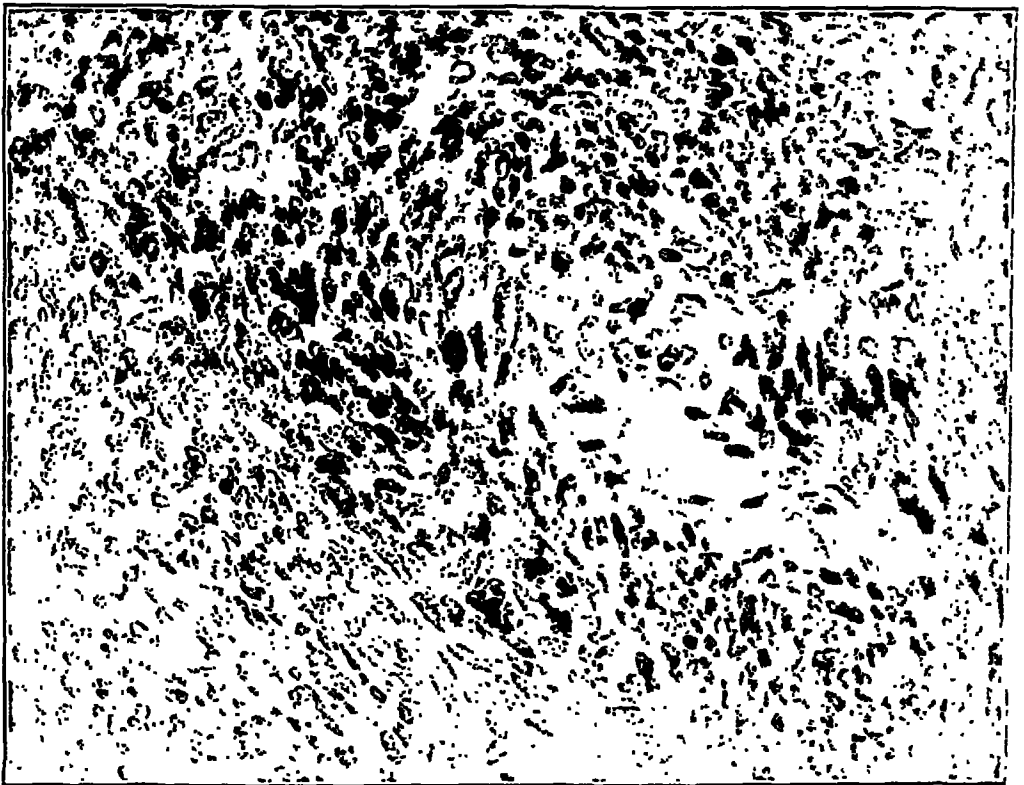


Fig. 6 (case 1).—High power magnification of first recurrence. The glandular elements are being crowded out by the embryonal character of the stroma cells.

and fat were retracted. The ulnar nerve, prior to its entry into the pronator teres, was exposed and the nerve followed down to a point where it was lost in the tumor mass just above the internal condyle. The skin flap was then dissected away from the muscle, exposing the biceps and the tumor mass, which was covered by the flexor muscle originating from the internal condyle. The brachial artery was then retracted medial to the ulnar side, exposing the median nerve below. We then followed the median nerve to its point of implantation into the ulna by cutting through the pronator teres and palmaris longus muscle belly. We could see the suture line as evidenced by the black silk which had been used a year ago. There was apparently no thickening of the exposed portion of

When last heard from, four years after operation, he weighed 200 pounds (90.7 Kg.) and was in excellent health.

Summary.—1. A patient with von Recklinghausen's disease presented a tumor of a peripheral nerve.

2. The tumor resembled a carcinoma. It was made up of glandlike spaces lined by columnar cells with little separation of the individual cells, which gave the appearance of a syncytial mass. Mitoses were noted.

3. After excision of the tumor, recurrence occurred in the stump.

4. Histologically, this resembled the primary tumor.

5. A second recurrence necessitated amputation.



Fig. 9.—Low power magnification of first recurrence tumor of the radial nerve.

6. This tumor contained spindle-shaped cells. There were small cavities which were lined with a single layer of cells resembling epithelium.

7. The patient remained well for at least four and one-half years. Since that time, we have been unable to trace him.

8. The tumor was epithelial.

9. It caused expansion of the nerve and disturbance of the peripheral distribution of the nerve.

10. There were no distant metastases.

Certain questions naturally arise: 1. What is the origin of a tumor of the nerve which is epithelial? 2. Is it part of a systemic disease? 3. What is its relation to von Recklinghausen's disease? 4. Did it come

grayish white and apparently made up largely of supportive tissue. The bands of tissue running in all directions gave somewhat the appearance of a leiomyoma of the uterus. The blood vessels were not prominent, and only here and there were areas noted which appeared to be well supplied with blood. An occasional area on the cut surface was noted which showed degeneration suggestive of a myxomatous or loose, meshlike type of structure containing a clear pinkish stained serum, but no definite lobulation or cystic cavity could be found.

Microscopic study showed the mass to be almost uniformly made up of spindle-shaped cells running in bundles in all directions. Some of these strands were considerably older than others and tended to separate the more rapidly growing ones into distinct areas. Here and there little microscopic cavities could be noted



Fig. 8 (case 1).—Patient several months after amputation.

that were lined with a single layer of cells resembling epithelium. The blood vessels were not prominent in the main portion, although here and there a few capillaries were noted. Some of the older portions of the growth showed considerable deposition of collagen-like material, and still others were somewhat myxomatous. Many of the cells were rapidly growing and showed mitotic figures. The histology was that of a neurogenic sarcoma, with absence of the glandlike spaces noted in the primary growth.

Progress Notes.—On June 29, the wound was dressed. Swelling was not so great. Primary union occurred and the patient was permitted to go home, but was kept under observation for more than a year. His general condition continued good with no evidence of recurrence or development of the tumor in any other location.

After twenty years of experimental observations (1904-1924), Harrison³ stated:

One who follows historically the subject of the histogenesis of the nervous system cannot but be impressed by the deviousness of the path of progress.

With the foundation of the neuron theory by His (1886) and Forel (1887) the study of the nervous system entered upon its modern phase.

The investigation of His (1886, 1887, 1888, 1890) followed by the work of Ramon y Cajal (1890, 1892, 1894), who first applied the Golgi method to the study of the embryonic nervous system, and that of v. Lenhossek (1892, 1895), gave a firm footing to the concept of the neuron by showing clearly, as it then seemed, that each fiber arises as the outgrowths of the single ganglion cell.



Fig. 10.—High power magnification of first recurrence.

Experiments, with hanging-drop cultures of embryonic nervous tissue in clotted lymph, rendered possible the direct observation of the growing nerve fiber, showing the latter to be not a chain of cells, but a strand of hyaline protoplasm with an active amoeboid end, through the motion of which the fiber is spun. In other words, it was actually seen that nerve fibers grow as the process of a single neuroblast.

To sum up the impression gained from the study of the relevant literature accumulated since 1900, we find that the neuron concept, so far as it applied to the development and regeneration of the nervous system, remains unshaken under the attacks it has received, and that it now stands more firmly established than ever.

3. Harrison, Ross G.: Neuroblast Versus Sheath Cell in the Development of Peripheral Nerves, *J. Comp. Neurol.* 37:123 (June) 1924.

from a misplaced cell rest or can it be explained by referring to the histogenesis of some element of nerve tissue?

Tumors of the peripheral nerve must originate (1) from some constituent of the nerve; (2) from misplaced cells; (3) be part of a systemic disease, or (4) be metastatic growths.

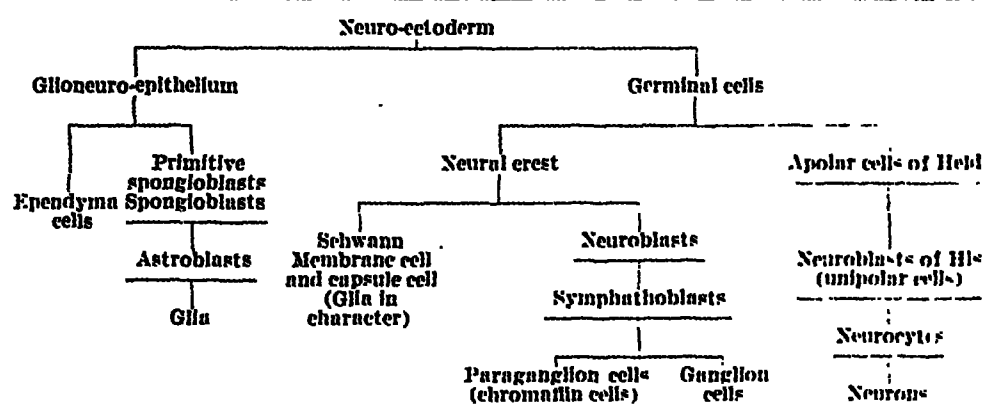
To develop the subject, it will be necessary to introduce a brief review of the embryology of the nervous system and the facts as well as the theories available in the literature.

Some of the following data are essentially academic, but necessary to present the subject clearly.

Embryology.—According to Hardesty: ¹

The essential elements of the nervous system, the nerve cell-bodies and the essential portion of all nerve fibers, central craniospinal and sympathetic, develop from one of the embryonic germ layers, the ectoderm, and all arise from a given

Histogenesis of Nervous System (Glober and Strauss)



region of that layer. Further a small portion of the supporting tissue of the nervous system the neuroglia, is of the same origin.

Peripheral Nerves.—According to Stookey: ²

A typical peripheral nerve is made up of neuraxes from nerve cells either within the brain stem and spinal cord, or from cells of the spinal, cranial and sympathetic ganglia.

Two main theories have been offered concerning the origin of the neuraxes, one the outgrowth theory of His (1890) and the other the cell chain theory of Bethe (1903) and others. A still older theory is that of Henson, according to which there always are protoplasmic intercellular bridges in the developing embryo and out of certain of these bridges the nerve fiber is differentiated. Held (1909) has supported a modification of this theory, according to him the nerve fibers differentiate from the nerve cell bodies along these protoplasmic bridges.

1. Hardesty, Irving: The Development of the Nervous System, in Morris' Human Anatomy, Philadelphia, P. Blakiston's Son & Company, p. 754

2. Stookey, Byron: Surgical and Mechanical Treatment of the Peripheral Nerves, Philadelphia, W. B. Saunders Company, 1922.

Both medullated and nonmedullated fibers are assembled in nerve bundles called funiculi, and the funiculi in turn are joined together into a larger group by a surrounding sheath of connective tissue called epineurium, thus forming a peripheral nerve. The individual fibers of the funiculi are separated by a small amount of connective tissue called endoneurium and the funiculi are surrounded by a lamillated layer of fibrous tissue which encircles the funiculi, called by Key and Retzius (1873) perineurium.

The origin of the cells of the sheath of Schwann has been a cause of great controversies.



Fig. 12.—Upper surface of dura.

Two main views have been held concerning the origin of these cells it being formerly thought that the sheath was of mesodermal origin. The more recent view on the other hand has been that the sheath cells were closely related to neuroglia and were of ectodermal.

The latter theory has been proved by Harrison's ganglion excision experiments.

By excising the ganglionic crest of young amphibian embryos peripheral motor nerves, in the form of naked axis cylinders, developed in place of nerves which normally had numerous spindle shaped sheath cells about them.

The experiments leading to this conclusion have recently been repeated by Muller and Ingver (1921) with like results.

The problem before us is, simply how the axon is constituted in development—whether it takes origin from a cell chain, or is the process of a single ganglion cell.

The method of procedure was to eliminate by appropriate operation first the source of the sheath cells, and, second, that of the motor ganglion cells.

The development of the axon is a function of the neuroblast.

The removal of any body of neuroblasts invariably results in the elimination of the peripheral nerves normally connected with them.

I may therefore proceed with the study of the development of the peripheral nerves, accepting as a proved fact that the neuraxis or axon is a product of the neuroblast, and continue to construct my concep-



Fig. 11.—Dissection of amputated limb.

tion of the development of the remaining portions of the peripheral nerve.

According to Stookey:

The neuraxis extended without interruption from the cell of origin to its ultimate termination. It consists of neurofibrils imbedded in a semifluid neuroplasm and surrounded by a very delicate membrane, the axolemma. The fibers are described as of two types, medullated, and nonmedullated, depending upon the presence or absence of a sheath known as a medullary or myelin sheath. The medullary sheath contains myelin—a chemical substance made up largely of lecithin, and supported by a framework or neurokeratin. Outside of the myelin is a delicate nucleated sheath known as the sheath of Schwann or neurolemma. The nonmedullated fibers of the peripheral nerves arise from the cells of the sympathetic and spinal ganglia.

The outstanding point today is the origin of the "connective tissue which immediately surrounds the nerve elements." Is he referring to the sheath of Schwann? That the type of cell which is its progenitor is ectodermal has apparently been settled by the experimental work of Harrison.

In 1908, Verocay⁶ studied a specimen from a case in which he had performed the autopsy. The case presented "multiple tumors in the central nervous system and its meninges as well as in the course of the peripheral nerves." He presented the case hoping that it may help in



Fig. 16.—Tumor involving entire right lung showing occlusion of bronchus.

this way to clear up a rather obscure field in the pathology of the nervous system.

His expectations have been more than realized, because all students of this subject refer to him as the first to express the idea of the association of peripheral and central nerve growths and the ectodermal origin of these peripheral tumors (sheath of Schwann).

He said:

The old dispute over the nature of Schwann's cells has at present been settled by showing that they are of ectodermal origin and that they originate from the same anlage as the specific nerve cells-nerve cells and glia cells.

6. Verocay, Jose: Multiple Tumors as a System Disease of the Nervous System, *Festschr. f. Hans. Chiari*, 1908, pp. 378-415.

Harrison said:

The sheath cells are best interpreted as a sort of peripheral neuroglia—an idea that has found favor with a number of students of the structure and development of the nervous system.

The sheath cells are clearly separated elements, which are closely applied to the axons. While they have but a small amount of cytoplasm, they are in no sense mere nuclei and part of the axon itself.

It is likewise definitely shown that the sheath cells are not mesodermal, but arise for the most part from the ganglion crest in connection with the spinal ganglia. Some arise later directly from the medullary cord by emigration along the ventral roots.



Fig. 13.—Gross photograph of brain with dura reflected showing neoplasm pressing on cerebrum.

The sheath cells are to be regarded as the neuroglia of the peripheral nerves.

The literature makes one feel justified in accepting the ectodermal origin of the cells of the sheath of Schwann.

When one turns to clinical experiences, one finds a state of confusion. If Harrison's work is correct, this confusion should cease to exist.

Pathology.—Is it possible for an epithelial recurring type of tumor of a peripheral nerve to arise from the elements of peripheral nerve, and may it be a part of a systemic disease, or must it be of metastatic origin?

Serre's paper must be freely abstracted:

The history of neurofibromatosis dates back to Recklinghausen who, in 1882, undertook the synthesis of the sparse findings in the previous observations of dermatologists, surgeons, and anatomic-pathologists.

The histologic conceptions of neurofibromatosis have varied greatly during the course of the last few years. After Virchow, who distinguished pure neuromas mixed neuromas (true neurofibromas) and false neuromas (fibro-myxomas, fibrosarcomas), Recklinghausen, in 1882, grouped all the cases under the heading of fibromas.

To this purely connective conception in which the tumors were considered as being derived from the perineurium, Bard, in 1885, opposed a theory, sanctioned by Durant in which the neurofibroma was derived from the segmentary cell of the nerve fiber. With the investigations of Held and Nageotte on the histology

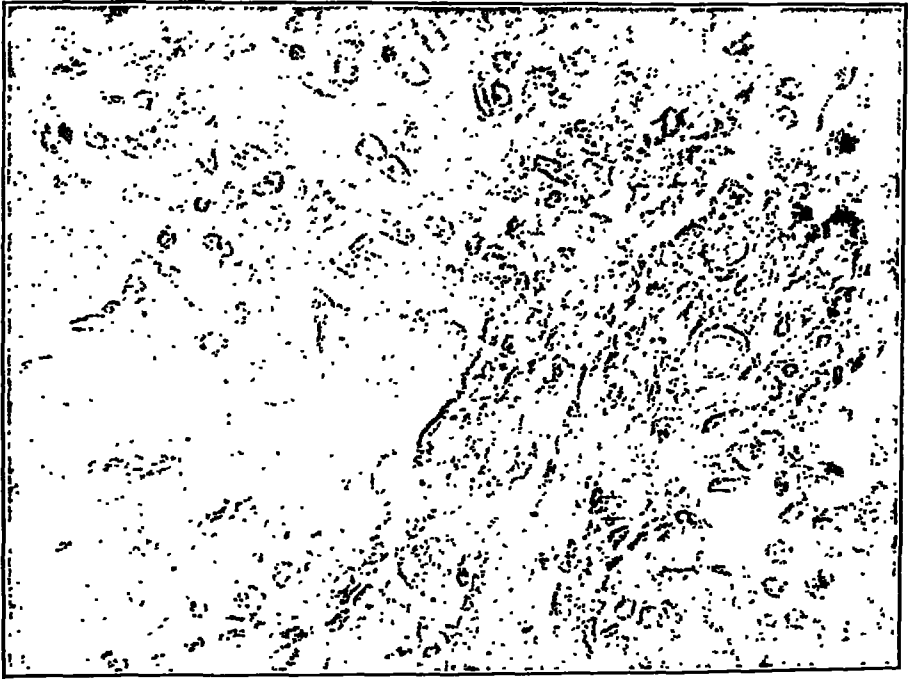


Fig. 18.—High power magnification of tumor of lung.

of the nerves and the works of Verocay, Trapier, Bard, Gall, Gautier, Delore, and especially with the recent studies of Lhermitte and Leroux, there has arisen the new theory of peripheral neurogliomatosis developing at the expense of the sheath of Schwann or the peripheral neuroglia.

Discussing Recklinghausen's disease, he said:

Lhermitte and Leroux state that the constitution of the peripheral tumors in Recklinghausen's disease has the fundamental characteristic of being formed by the combination of two tissues, one a compact tissue resulting from the juxtaposition of fusiform cells, the other more loose and reticulated formed of cells with ramifying protoplasmic expansions which anastomose together.

The compact tissue is formed of fusiform elements parallel to each other forming trabeculae, whorls and bundles. The cell itself has a regular ovoid

He summarized as follows:

The above case was an extensive system disease of the central and peripheral nervous system and its meninges in the form of the multiple tumors of the spinal cord and medulla oblongata (glioma) the nerves (originating from the nerve fiber cells and the connective tissue?) and meninges (endothelioma).

2. This system disease is with great probability to be attributed to a congenital anomaly of development.

3. Tumors of the nerves occur with the picture of "Neurofibromatosis" (fibromatosis-nervorum) or "True multiple neuromas which originate from the so-called nuclei of Schwann's sheath, for which reason they are to be regarded as nerve tumors.



Fig. 17.—Low power magnification of tumor of lung.

4. These nerve tumors may also contain ganglion cells the presence of which seems to be most easily comprehensible if they are regarded as being derived from nerve fiber cells also in the normal development of the sympathetic.

Serre⁷ presented two cases with peripheral tumors. He expresses the following positive opinions relative to several questions at issue in cases of tumors of peripheral nerves associated with Recklinghausen's disease: 1. These tumors originate from sheath of Schwann. 2. They are part of a systemic disease. 3. Von Recklinghausen's disease is not mesodermal in origin, but the tumors are "developed at the expense of the sheath of Schwann and hence are of ectodermal origin."

7. Serre, R.: Contributions to the Study of the Visceral Localization of Recklinghausen's Disease, Thesis, Paris, 1923.

opposed to the appearance of clearly individualized adult connective tissue cells, the cytoplasm of which is never fibrillar.

These tumors in no way resemble fibroids from which they differ by the morphologic appearance of the cells, the vascular alterations and the necrotic areas.

Their cellular irregularities, their well individualized cells, the absence of vessels provided with true walls, their tendency to metastases, in a word, their characteristics of nonencapsulated malignant tumors differentiate them at once from the gliomas which are always encapsulated.

There is no point of equal contact between these peripheral tumors of Recklinghausen's disease and the connective tissue tumors. On the contrary there are four arguments which speak in favor of the neuroglial origin of these tumors.

1. The absence of cellular individualization, the syncytial appearance.



Fig. 20.—Low power magnification of tumor of heart muscle.

2. The collection of the fusiform cells into bands or whorls, resembling the appearance of gliomas forming after amputations.

3. The fibrillation of the protoplasm of the fusiform cells and the equally fibrillary structures of the stellate cells, similar to those seen in the gliomas of the brain (Lhermitte and Leroux).

4. The structure of the vessels, the walls thickened by the fibro-hyaline substance, the vascular obliterations.

We can conclude with Lhermitte and Leroux as to their ectodermic neuroglial, syncytial origin and can consider them as peripheral gliomas developing at the expense of the sheath of Schwann.

Conclusions: In Recklinghausen's disease the tumors are not of the connective tissue type of mesodermic origin. The tumors are all of the neuroglial type and are gliomas developing at the expense of the sheath of Schwann and hence are of ectodermic origin.

elongated nucleus surrounded by ill-defined protoplasm, separating the neighboring cells without cellular individualization, that is to say, the syncytial type. Finally a very important characteristic should be noted—the protoplasm is finely fibrillar.

The constitution of the reticulated tissue is very different from that of the compact tissue. Here the cellular elements are stellate cells with protoplasmic expansions more or less loose and anastomosing with the prolongations of the neighboring elements. The elements like the preceding, present a fibrillary protoplasm.

This general description seems to hold true for all the cutaneous and visceral peripheral nerve tumors of Recklinghausen's disease.

Nature of the Neoplastic Tissue.—Let us see now why these tumors may be mistaken for fibrous tumors of connective tissue origin and how they may be distinguished. There are three points to be considered: (1) the presence of



Fig. 19.—Tumor of heart and kidney.

collagen; (2) the morphologic appearance of the cells; (3) the disposition of the vessels.

Is collagen specific of connective tissue cells or vessels?

Up to the last few years it has been considered that the collagen framework of the connective tissue is an integral part of the connective tissue cell.

Lhermitte and Leroux have recently shown, in the case of an intra-ventricular echinococcal cyst, that there was precipitation of collagen in the middle of an adult neuroglia tissue.

In Recklinghausen's disease the presence of connective tissue cells cannot be concluded from the presence of collagen.

The morphological appearance of the cells is of capital importance. The cells of these tumors are formed of a protoplasm with indistinct outlines which is prolonged into a very fine fibrillary arborization anastomosing with the arborization of neighboring cells. Sometimes, even, the cytoplasm assumes a more clearly syncytial appearance and many clear nuclei may be found. Finally, under high magnification, the protoplasm is seen to be clearly fibrillar, this being

neoplasm, but our neoplasm did not show the characteristics of a neurogenic sarcoma until two previous growths had been removed.

The arrangement is very suggestive of epithelial origin, especially as the most actively growing cells are in glandular form.

The histology suggests very closely the histology of certain ependymal neoplasms. It is therefore necessary to resort to the theory that this neoplasm sprang from a cell which was carried down from the central nervous system in the development of the median nerve, it having its primary origin in the neuro-epiderm of the developing embryo.

Percival Bailey⁹ has described the typical ependynoma as follows:

The tumor is composed of a mosaic of polygonal cells with well defined cell borders and heavy, coarsely granular cytoplasm. The cells are crowded against

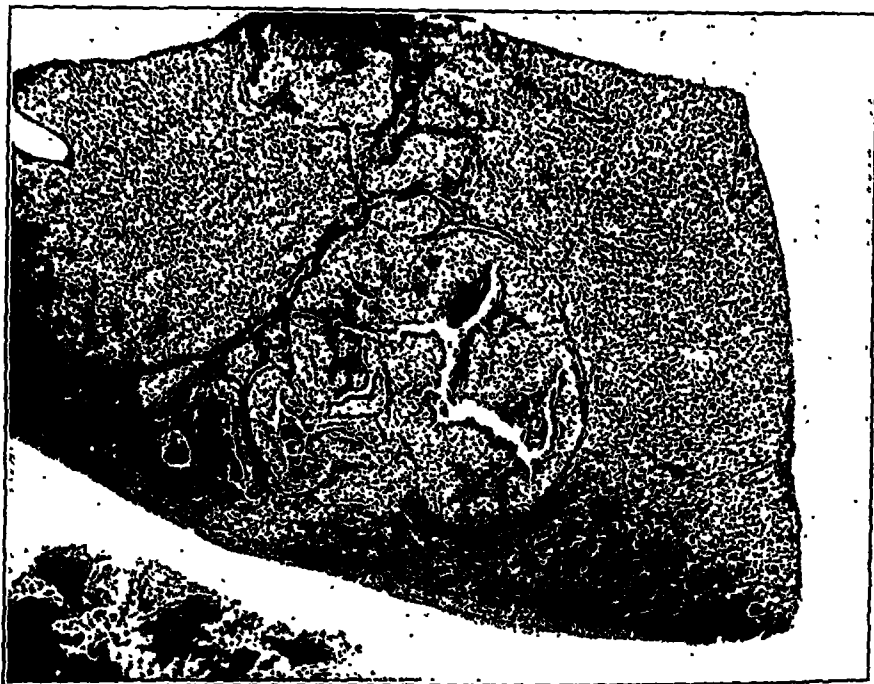


Fig. 22.—Low power magnification of tumor of kidney.

each other and have a single, large, vesicular nucleus. Among them may be seen a few coarse fibrils which stain poorly with methods for the demonstration of neuroglia fibrils. In certain areas the fibrils may be seen to be the continuation of one extremity of the cells. In these areas the cells are apt to have a tendency to arrange themselves radially around blood vessels or around channels whose walls contain a little poorly developed, often hyalinized connective tissue. No other connective tissue is present. In practically all the cells (probably all of the entire cells were included in the section) is to be seen a clear area containing sometimes one, usually two or three, rarely as many as a dozen small, clean-cut markings which stain heavily or by methods for demonstrating neuroglia fibrils, and may be spherical or short bacillus-like rods. These markings we have interpreted as blepharoplasten, or typical of ependymal cells.

9. Bailey, Percival: A Study of Tumors Arising from Ependymal Cells, *Arch. Neurol. & Psychiat.* 11:1 (Jan.) 1924.

Stout⁸ reported a case which presented certain points in common with my case. In discussing the case, Stout wrote:

Turning now to tumors arising in the peripheral nerves one is impressed with the fact that the literature is very scanty, but the majority of authors consulted seem to agree that whether single or multiple, malignant or benign, they are of mesodermal origin, coming from the epineural or perineural tissue. In 1906, on the other hand, Verocay described a case with multiple tumors of the nervous system which showed in many of the nodules in the peripheral nerves what he believed to be a marked growth of cells of the sheath of Schwann. He is thus the first author to suggest that the neurilemma cells may be the source of tumors of the peripheral nerves. This view is looked upon with favor by Borst writing in Aschoff's Text Book.

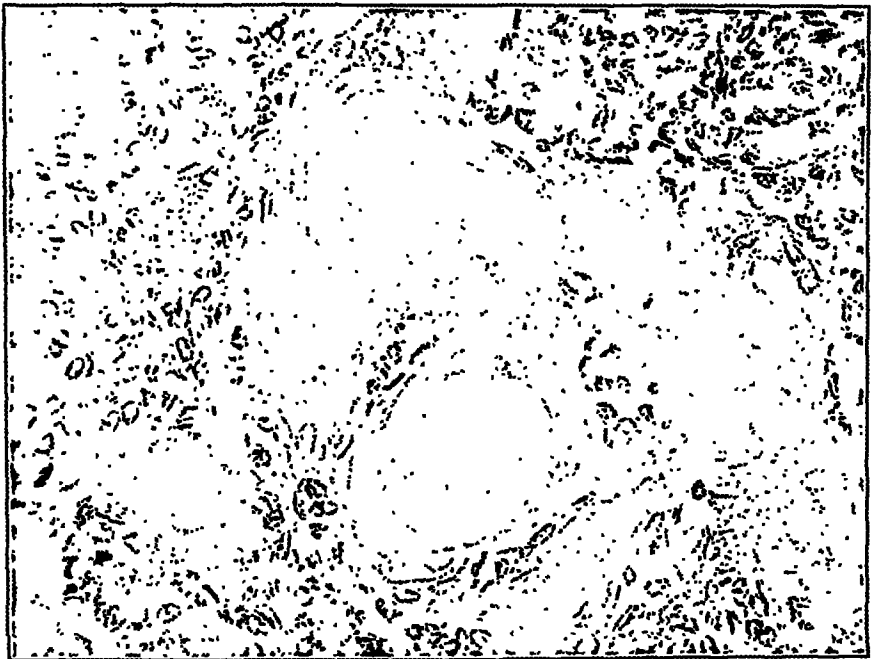


Fig. 21.—High power magnification of tumor of heart muscle.

In conclusion, it may be said that the tumor under consideration is a malignant neoplasm. Since the neurilemma of the peripheral cells is probably homologous to the neuroglia of the central nervous system it is suggested that this tumor may be a neoplasm arising from neurilemma cells or lemmocytes.

Lanford, in a previous report of this case, made the following observations:

Adami quotes Verocay to prove that the cells of the sheath of Schwann are of neuroblastic origin and that any tumor arising from the sheath is a neuroma. If this is true, we would be forced to include many of the tumors encountered in von Recklinghausen's disease and could find an explanation of the origin of our

8. Stout, A. P.: A Tumor of the Ulnar Nerve, *Med. & Surg. Rep. Presbyterian Hosp.*, New York, 1918, vol. 10.

There was a mass which extended up to the middle of the scar and downward at least $1\frac{1}{2}$ inches below the head of the radius. The mass seemed to be on the outer side of the biceps insertion. The skin moved freely over it. This mass was nodular, not painful and was movable in a lateral direction. Pressure on the mass did not produce any disturbance in the peripheral distribution of any of the main branches of the brachial artery. Apparently this mass did not have any deep attachment. Just above the external condyle and to the outer side of the triceps, there was a small nodular, firm mass which was not movable. The skin glided freely over the mass. I could not feel any axillary mass.

The patient was advised to have a roentgenogram of the chest made at once with the view of determining the operability.

He did not return until Dec. 31, 1926. At that time the following examination was made: On the outer side of the left elbow just lateral to the scar, the skin

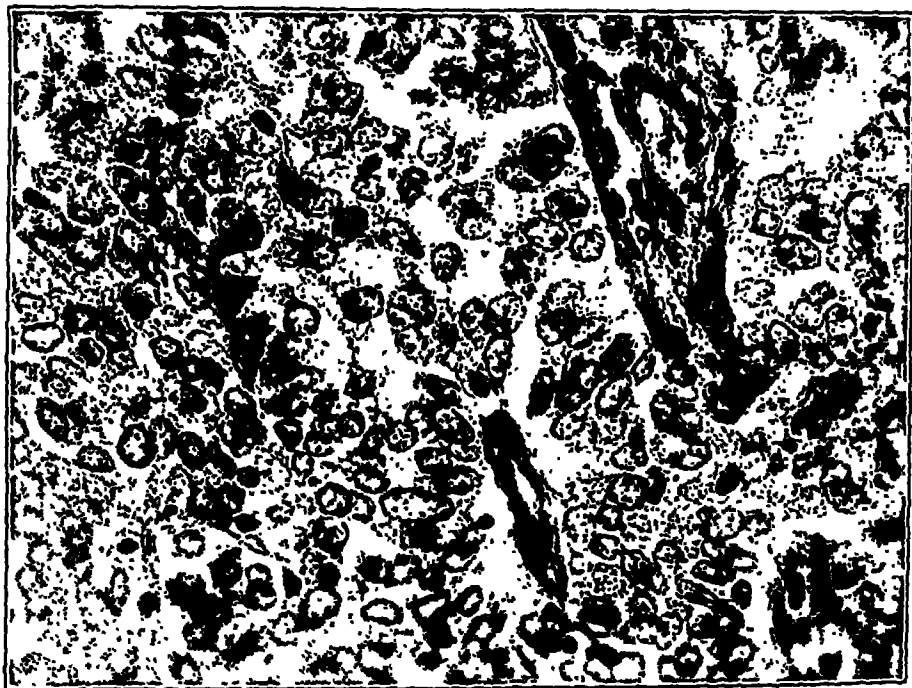


Fig. 23.—High power magnification of tumor in kidney.

had a bluish tinge. There was an irregular, nodular mass under this area. The level of the growth was four fingerbreadths below the external condyle and apparently under the supinator longus muscle. The upper limit of the mass was more than four fingerbreadths above the external condyle. The mass was movable in a lateral direction, but not up and down. The anteroposterior diameter of the mass above the elbow was about 2 inches. It was nodular, hard and painful. The mass extended upward along the upper border of the external condylar ridge of the humerus. There was limitation of extension of the arm, about 150 degrees, and flexion of 45 degrees. He was able to palmarflex and dorsiflex the wrist. Supination and pronation of the forearm were not impaired.

On the inner border of the biceps muscle, corresponding to about the middle of the arm in the course of the median nerve and brachial artery, there was a hard, nodular mass which was movable in a lateral direction, which was not movable up or down. It was not fluctuant. The size could not be diminished by pressure, proving that it was not a vascular dilatation, at least to my mind. Pres-

I can do no more than to leave this interesting tumor for further study by pathologists (Dr. Lanford and others) that it may eventually be properly catalogued.

Summary.—1. Recent investigations in embryology, particularly the work of Harrison, indicate that the sheath of Schwann is ectodermal in origin.

2. The clinical experience of Verocay and others indicate that neoplasms of the peripheral nerve arise from the cells of the sheath of Schwann.

3. These tumors of the peripheral nerve may be a part of systemic disease.

4. Recklinghausen's disease is not mesodermal in origin.

5. Penfield's work would indicate that he is in accord with these statements.

6. Epithelial neoplasms of peripheral nerves, when part of a systemic disease, may recur in the remains of the nerve, but they do not cause involvement of the lymphatics.

7. If recurrence occurs, amputation may be the only means of cure.

8. I believe that this tumor had its origin in the cells of the sheath of Schwann.

EPITHELIAL NEOPLASM OF THE RADIAL NERVE ASSOCIATED WITH
NEOPLASMS OF LUNG, HEART, LIVER, BRAIN, DURA,
CALVARIUM AND SUPRARENALS

CASE 2.—History.—Mr. J. J. G., aged 53, complained of symptoms which began in June, 1926, when he first noticed a hard lump in the "crease of the right elbow," which increased in size. On October 22, under local anesthesia a portion of the mass was removed by Dr. Metz. The mass recurred and became larger than before. He experienced pain, but function was not disturbed.

In March, 1926, he was told that he had tuberculosis, because of a cough and a purulent expectoration which was streaked with blood.

Examination.—Examination was made on Dec. 13, 1926. There was a scar about $2\frac{3}{4}$ inches long on the lateral aspect of the right elbow. The skin on either side of this scar presented nothing of note. The right elbow was larger than the left elbow. There was apparently a diminished carrying angle and fulness in the antecubital fossa. The difference in size of the two forearms extended down to the wrist. The hand, on the palmar aspect, seemed slightly purple, in fact, the whole hand presented a mild cyanotic hue. When asked to pronate the forearm, he lifted the palm of the right hand up with the left; he called my attention to the fact that he was able to pronate the hand without the aid of the opposite hand, and demonstrated that fact.

There was tenderness and a noticeable difference in the size of all of the fingers, those of the right hand being slightly larger than the left. The muscles of the forearm were flaccid. The skin showed no difference in temperature. Palpation revealed all sensations present.

A circular type of incision was made. When the cuff of skin was retracted upward, the brachial artery was ligated. The axillary vessels were ligated. The median, ulnar and musculocutaneous nerves were cut high, and they were then "fish-tailed."

After this, the muscles were cut above, 1 inch higher than the skin cuff, the bone sectioned higher and the tourniquet released. Bleeding was not encountered. The muscles were quilted over, and the skin closed with interrupted dermol and fine continuous lock stitch.

The specimen was sent to the pathological department for inspection, section and dissection, and the following pathologic report was made: The axillary vessels lay on top of the median nerve and were closely adherent to the nerve. There was a groove on the inner aspect of this tumor mass made by the vessels. The median nerve could be dissected practically free from both vessels and the



Fig. 25.—Suprarenal gland, low power magnification of tumor.

tumor. The tumor mass measured 3 by 1.5 by 1 cm. It was irregular and nodular. In places, it seemed to have broken through its capsule and was adherent to the surrounding tissue. On the outer side of the growth and overlying it was a large nerve trunk mass. Peripheral branches of the nerve were seen coming out of the lower nerve of the tumor mass. Along the vessel which accompanied the radial nerve small but similar masses were found. The wall of the vessel at this point seemed thicker as though it contained some new growth. There was a mass lying under the supinator longus muscle, which was about 6 by 3.5 by 2 cm. The upper portion of the muscle was normal in appearance, but the mass seemed to have invaded it. It was nodular and grayish. The radial nerve was dissected down and followed into the growth. Above the level of its penetration there was a small nodule; this mass seemed to be of the same character as the rest. The radial nerve below the muscle was dissected down to the wrist and was seen emerging from the mass, while the nerve itself was smaller than expected normally. The supinator longus was sectioned in its most prominent point and

sure over this mass did not produce any disturbance in the peripheral distribution of the median nerve. Palpation in the axilla did not reveal any mass.

He was advised that "nothing short of a high amputation is going to be of any service."

Progress Notes.—Jan. 1, 1927: The patient was admitted to hospital for observation. The mass on the right arm, along the course of the radial nerve, was probably a malignant tumor of the nerve. He had a cough and raised bloody sputum. A roentgenogram of the chest was taken.



Fig. 24.—Liver showing metastatic tumor.

January 2: Roentgen-ray examination showed what was taken to be fluid in the right side of the chest with some pleural thickening.

January 3: An operation was performed. A diagnosis was made of recurring and metastizing epithelial neoplasm of musculospiral nerve; metastasis had occurred to the median nerve.

The radiologist reported that "there was no evidence of metastasis to the chest."

Operation: The arm was amputated. Wyeth pins were introduced in the front and the back and in the upper limit of the axilla, and a rubber tube tourniquet was used.

January 9: Hemoptysis occurred again in the afternoon. There apparently was an ounce of blood.

January 10: The dressing was changed in the morning. The patient still complained of some pain. A small amount of blood was present in the sputum throughout the day. The patient said that the lump in the top of his scalp was larger.

A consultation with Dr. Lemann, chief of the medical service, was asked. He reported "It is my impression that there is fluid in the pleural sac and I would recommend exploration with a syringe. In spite of suggestive history of preceding tuberculosis, I am inclined to believe we are dealing with a pulmonary metastasis."

January 11: A laboratory report showed that the sputum was examined twice; tubercle bacilli were not found, but gross blood appeared both times.

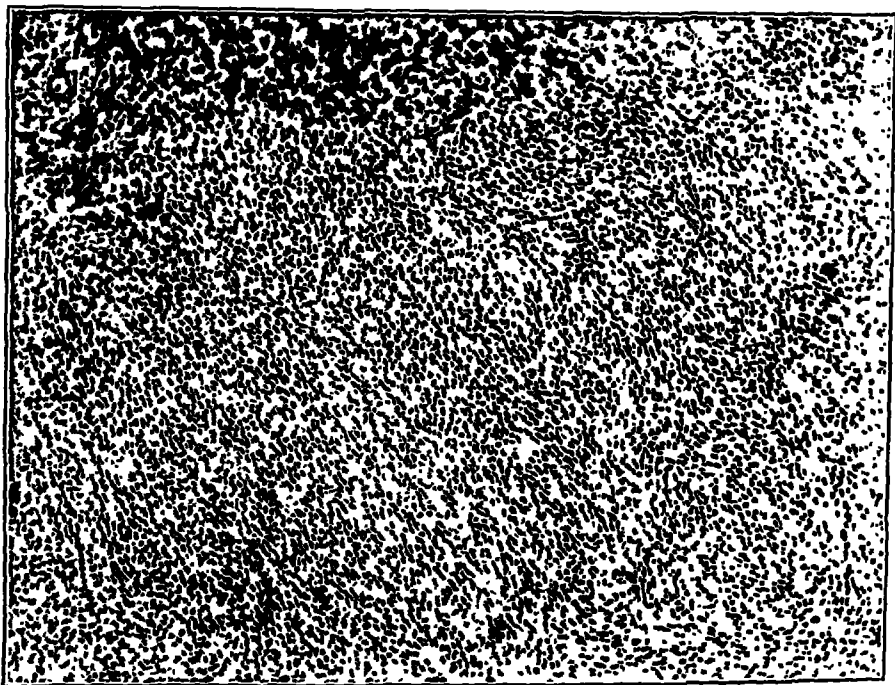


Fig. 27.—Tumor of spinal accessory nerve; low power magnification.

January 12: Profuse hemoptysis occurred in the morning. One-quarter grain (0.016 Gm.) of morphine was given twice, and 5 cc. of 10 per cent calcium chloride given intravenously.

January 13: The patient spat a little blood in the evening, for which morphine was given with good results; 5 cc. of calcium chloride was given intravenously.

January 14: The patient spat blood; 5 cc. of 10 per cent calcium chloride was given intravenously in the evening.

January 15: He did not spit blood. The dressings were changed and the sutures removed. The wound healed, with primary union. Five cubic centimeters of 10 per cent of calcium chloride was administered intravenously.

January 17: He had been spitting blood-streaked sputum the day before but morphine was not given. Five cubic centimeters of 10 per cent calcium chloride was given on that day and 5 cc. calcium chloride the following day.

January 18: The sputum was still streaked with blood.

January 19: The wound was dressed, and the patient allowed to go home, improved.

the tumor mass exposed. The cut surface varied from pink to gray and was rather uniform, with the exception of a number of areas of small yellow comedones that exuded on slight pressure. The under portion of the cut sections showed rather distinct lobulations, especially where they had encroached on and distended the muscle. Blood vessels were not a prominent feature. There was an irregular and nodular mass, measuring 7 by 5 by 2.5 cm. which sprang upward on the lateral side of the triceps tendon. When cut, it presented exactly the same appearance as the outer tumor.

A section was taken from the neoplasm involving the supinator longus, triceps and in the bicipital groove epithelial neoplasm presenting islands of embryonal cells, the centers of which showed keratinization. The young cells were somewhat columnar, and a few groups showing a suggestion of glandular arrangement surrounding new growth was suggestive of glia tissue (Lanford).

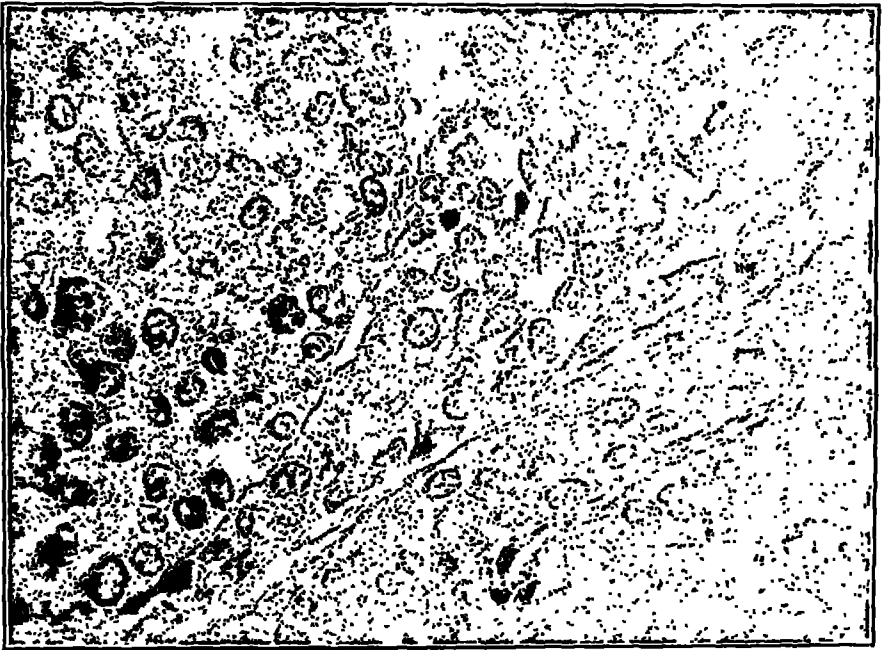


Fig. 26.—High power magnification of tumor of suprarenal gland.

On January 3, the roentgen-ray report stated that the left side of the diaphragm was smoothly contoured, the right obliterated. No increase in the size of the cardiac or great shadows was visible. In the upper reaches of the left side of the chest, small fan-shaped density was observed which was considered to be suggestive of an early tuberculous lesion. The same type of fluffy shadow was visible in the upper right side of the chest, and the changes were scarcely sufficient to warrant a positive diagnosis. In the base of the right lung, the diaphragm was obliterated, and a definite, fairly large density was observed of the type commonly seen when fluid obliterates the base. The pulmonary changes were insufficient to form the basis for a positive diagnosis of tuberculosis, although this must be considered as probable, but a neoplasm producing fluid cannot be ruled out. Consultation with the clinician was requested (Henderson).

On January 7, in the afternoon, the patient spat up a large amount of bright red blood and blood-stained sputum throughout the night. Hemoptysis occurred in the morning.

There was some bulging of the right side of the chest and a flatness of the whole right side of the chest. Râles were not heard, and the respiratory sounds were clear. The voice sounds were transmitted, not distant, but, if anything, intensity was increased. At the base, the voice sounds were distant and there were no râles. The mass in the side had not increased in size. The patient continued to expectorate blood freely.

March 19: At 6 o'clock, the patient had a coarse tremor of the left arm, the left leg and the left side of the trunk. This coarse tremor was accompanied by a fibrillary tremor of the fingers of the left hand.

There was a decided deviation of the angle of the mouth to the right and also a widening of the left palpal fissure. The weakness of the whole left side seemed to be becoming more prominent.

March 20 to 24: The patient was unable to raise his left arm. If the arm was elevated and the supporting force removed, the patient's arm dropped to the bed. There was a coarse convulsive movement of the left side (upper and lower extremities). The right pupil was dilated. Respiration was irregular, and the pulse became markedly irregular. There was progressive difficulty in swallowing as well as progressive stupor.

March 24: The patient died.

Autopsy Report.—Postmortem examination was made on March 25. The body was that of a white man measuring about 170 cm. in length and weighing about 140 pounds (63.5 Kg.). The head was covered with a full suit of black hair. The right arm had been amputated at the shoulder joint, and the scar was well healed. There was a scar on the abdominal wall about 1 inch from the midline extending along the costal border for 3 inches. There was an irregularity in the scalp corresponding to a firm irregular tumor mass that had extended entirely across the skull from one temporal ridge to the other; it involved about one half of the parietal bone anteriorly and extended backward to the occipital ridge.

When the peritoneal cavity was opened the gallbladder was found adherent to the wall; a number of adhesions were also found between the liver and the diaphragm; these were firm, but fairly easily broken up. The liver extended about two fingerbreadths below the costal border. There was no evidence of inflammation of the general peritoneal cavity. The appendix was retrocecal and showed a number of old adhesions. The cecum was found to be slightly distended, and the transverse colon was very much so. There was a small band of adhesions which were firmly contracted and empty. The lesser peritoneal cavity was normal. The lymph nodes were not enlarged.

When the sternum was removed, it was found to be adherent on the right side to the underlying structures of the right pleural cavity. The left pleural cavity was completely obliterated by firm adhesions between the wall and the lungs.

When the heart was removed, a cellular mass was found in the posterior portion of the sac. This was particularly striking between the entrance of the inferior vena cava and the superior vena cava. The mass involved the right lung and almost completely obliterated it.

The heart was flabby in consistency and dilated. The outer surface was pinkish red, and on the right ventricle there was a large soldier's patch. An irregular nodular secondary neoplasm was noted in the wall of the left auricle and a similar nodule in the wall of the right auricle. The endocardium was smooth, there being nothing within to correspond to the new growth on the epicardium. The attached portion of the aorta was the seat of a rather

He returned on February 24 because of persistent headaches.

Examination showed a circumscribed, hard mass which was movable with the skin of the scalp.

On the right side of the abdomen on the outer border of the right rectus, there was a small circumscribed, hard, slight movable, painless mass about 1 inch (2.5 cm.) in diameter. This mass did not increase in size when the patient coughed, nor was it reducible into the abdomen. The patient was advised that it was impossible to tell the exact nature of the condition without operation. In view of the facts of his past history, I advised removal.

The wound on the stump was entirely healed. No mass was palpable in the stump. The skin over the axilla and the stump was freely movable. There was nothing to suggest a recurrence or metastasis of the axilla.

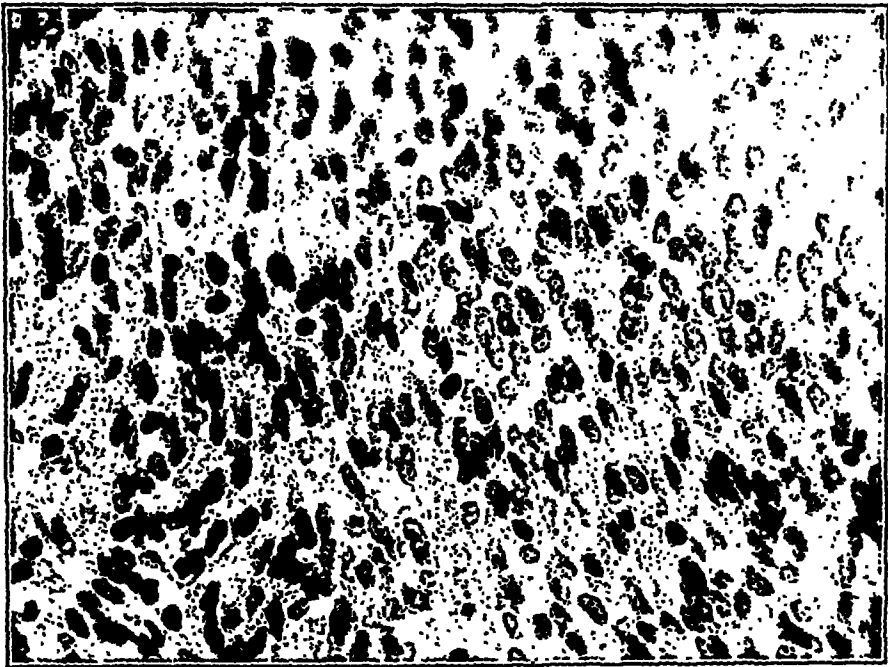


Fig. 28.—High power magnification of a tumor of the spinal accessory nerve.

Second Operation.—March 8, 1927: The preoperative diagnosis was tumor of the scalp and the abdomen. A diagnostic incision was made. In making preoperative diagnosis, the question arose as to whether we were dealing with metastasis from the original growth, or whether it was a cyst of the scalp.

An incision about 2 inches long was made over the most prominent portion of the tumor of the scalp. As soon as the skin had been reflected, we saw a solid tumor. We immediately realized that we were dealing with a malignant growth, and decided to remove a small portion for section. This was done and a specimen sent to the pathological department.

March 10: Since the operation, the patient had been restless and had complained that the weakness on the left side had been progressive. He lifted the left arm and forearm from the bed with difficulty. When the forearm was lifted up and the supporting force removed, the hand dropped. He had little grip. Loss of sensation in the distribution of the brachial plexus of the left side was noted.

was forcibly removed, it was found that the superior longitudinal sinus was free from involvement; the falx cerebri was also free of new growth. Sectioning of the brain showed the right cerebrum deeply infiltrated by the tumor mass for a distance of 1 inch in the middle portion of the parietal lobe and $1\frac{1}{2}$ inches in the posterior portion; the new growth had extended over and pressed on the motor areas of the right side. The left side of the cerebrum was not infiltrated, the new growth being confined to the pia-arachnoid. The ventricles were normal.

The anatomic diagnosis was: carcinoma of the lungs and mediastinum; secondary carcinoma of the skull involving the dura; secondary carcinoma of the brain; secondary carcinoma of the kidney; secondary carcinoma of the liver; secondary carcinoma of the suprarenal; secondary carcinoma of the heart and pericardium; lobular pneumonia; chronic pleuritis; chronic splenitis; healed tuberculosis, pulmonary; toxic nephritis; dilatation of the heart, and acute splenitis.

The microscopic diagnosis was: squamous cell type carcinoma in the dura; brain, squamous cell type; in the suprarenal, secondary carcinoma with marked albuminous degeneration in the cortex; pancreas, normal; kidney, cloudy swelling, albuminous deposits and degeneration and chronic interstitial nephritis; spleen, chronic splenitis, passive congestion and amyloid deposits.

Summary.—1. This patient had a cough, hemoptysis and profuse purulent expectoration.

2. He had been treated for several months for tuberculosis.

3. He presented himself for examination after a tumor of the radial nerve had been excised.

4. The recurrent tumor at the original site was larger than the primary growth.

5. Roentgen-ray reports indicated fluid in the chest, without evidence of metastasis to the chest.

6. An amputation was performed.

7. A tumor of the scalp was later found to be malignant.

8. Prior to death, the patient developed progressive weakness of the left side of the body.

9. Autopsy revealed a carcinoma of the right lung, carcinoma of the skull, dura, brain, kidney, liver, suprarenal, heart and pericardium.

"All tumors resembled epithelioma, all, except the nerve tumor could be classified as carcinomata." (Lanford).

The difference between this and the first case is apparent.

Where was the original growth?

By searching the literature I found certain clues which may help to identify the present growth.

Is this a neurocytoma—neuroblastoma beginning in the suprarenals, or is it a metastatic carcinoma with the lung as the site of the primary tumor?

Like Marchand, it will have to be admitted at the outset that much that is hypothetical will have to be stated. If a mistake is made others will eventually correct our error.

early arteriosclerosis, small yellowish elevations being noted. The coronary vessels were markedly thickened, and in places, almost occluded.

The right lung was small and almost entirely obliterated by a new growth. The lower lobe was most involved. Attached to the lung and the bronchus, there was a large mass of lymph nodes which were almost entirely replaced by new growth. On section, the lobe was found to be practically destroyed and replaced by a cellular pinkish-gray structure containing a few areas of necrosis. The blood supply of the part was relatively scant. A small abscess cavity was found filled with pus. The upper lobe was the seat of many spots of new growth. The left lung was doughy and rather uniform throughout, no firm nodules being detected. In the apex, there was an area of tuberculosis, and posteriorly, an area of lobular pneumonia. A slight amount of fluid exuded on pressure.

The liver was slightly increased in size and relatively firm throughout. The dome on the right lobe, however, showed an area of increased consistency, but the outer surface over this area was smooth. In the lower portion of the left lobe, there was another area of increased consistency which had a rough and irregular outline and measured about 3.5 cm. in diameter. It was yellow. Throughout the entire anterior and superior surfaces of the liver were a number of tags of adhesions. On section, an enlarged tumor mass was found occupying the upper portion of the right lobe, measuring about 7 cm. in diameter. The tumor mass on section had a serrated irregular outline, and the cut surface was uniformly dirty yellow with a number of spots of necrosis.

The spleen was small and bound down by a few adhesions. It was flabby and slate gray, except a long irregular area of congestion across its anterior third. On sectioning, chronic splenitis was revealed, and some slight increase in the pulp was noted. Grossly, there was no secondary neoplasm.

The kidneys were slightly increased in size and rather flabby. They were more or less uniform throughout, except that in the left kidney there was a mass on its outer edge somewhat increased in density and oval in outline. On section, the entire cut surface was found rather uniform in appearance and presenting the picture of a toxic nephritis, and the area of increased density corresponding to a secondary growth. Several other areas of new growth were noted. The right kidney presented a similar picture but careful study failed to reveal any secondary neoplasm.

The right suprarenal was flabby, and an area of increased density was found, irregular in outline; on section this appeared to be a neoplasm. It was definitely within the border of the suprarenal and had destroyed it. The gross appearance of this new growth was the same as that of the new growth in the outer organs. The left suprarenal was normal.

The testicle was free from a new growth. The bladder was filled with cloudy urine. The prostate was normal, and no evidence of neoplasm, either primary or secondary, was noted. The retroperitoneal space was free from any new growth. When the scalp was removed the tumor was found firmly adherent to and infiltrating the aponeurosis of the occipital frontalis muscle; palpation showed that it had destroyed the bones. The dura was firmly attached to the brain in the parietal portion by a tumor mass which had entirely infiltrated it. The tumor mass on its upper portion was rough, irregular, pinkish gray and contained spicules of bone by means of which it was continuous with the calvarium. There were several depressions in the superior surface of the external parietal lobe of the brain as a result of the new growth pressing down. The under surface of the brain was normal. The pituitary gland was somewhat swollen, but otherwise normal. When the dura

clinical and pathologic error in diagnosis, since the picture usually resembles some form of sarcoma and the tumor is as a rule diagnosed as such.

As Reisman points out, the failure to recognize the condition clinically may be due to the small size of the primary tumor, rendering it impalpable.

Meltzer¹² reported two cases:

CASE 1. Clinical History.—The patient, a man forty years of age complaining of severe stabbing pain in the left chest, shortness of breath, and cough. Roentgen-ray pictures showed opacity of the left lower chest to the level of the fourth rib anteriorly. A diagnosis of pleurisy with effusion was made.

Autopsy: The left lung was densely adherent to the chest wall, and when torn away no pus sac was discovered, but a great deal of degenerated, odorless material. This material came from the necrotic lower lobe, the greater part of which was occupied by a large tumor mass of a grayish color, with red and yellow patches of softening. This tumor measured 7 by 7 cm. in its greatest diameter. At the upper pole of the right kidney, just slightly invading the kidney substance was a rounded, firm, yellowish white mass, measuring 3.8 by 4 cm. Small portions of adrenal cortex were seen adhering to the tumor.

A soft hemorrhagic tumor, measuring 6 by 3½ cm. was discovered in the right frontal lobe.

Microscopic examination: The adrenal tumor consists essentially of diffuse deeply staining cells, interspersed here and there with bands of fine, pale, fibrils. The cells vary slightly in size, but the majority consists of a small dark rounded nucleus, with a very scanty cytoplasm in some, but in most no cytoplasm is evident. Other cells are pyramidal in shape with again practically no cytoplasm. Where the cells are crowded together densely the nuclei are elongated. Numerous mitoses are seen. A few very large cells, undergoing division, are present. The delicate fibrillar bands stain pink in eosin-hematoxylin sections. They do not possess the differential staining characteristic of neuroglia, fibroglia or collagen fibrils. The tumor is very vascular. Numerous thin-walled blood vessels are seen, and red blood cells lying free among the tumor cells. The "rosette" arrangement previously described is not observed.

In the lung tumor the same appearance is accurately reproduced.

CASE 2. Clinical History.—A man fifty-three years of age. Pain across upper abdomen, cough, and frequency of urination were complained of.

Autopsy: The body is that of a much wasted man with a very prominent abdomen. On opening the abdomen it is seen that practically the whole cavity is occupied by a hugely enlarged liver, which reaches to the right anterior superior spine. The liver weighs 11 pounds and is uniformly involved in a malignant process, being studded with tumor masses of varying size.

The right adrenal is of normal shape, but appears to be slightly enlarged. When cut into a small rounded tumor measuring 8 cm. in diameter is found to occupy the medulla. The cortex appears normal in the gross.

The lung is heavy and consolidated. The lower lobe is covered with a recent exudate. When the lung is opened a white mass 4 cm. in diameter and roughly spherical in shape is seen at the hilus. Several smaller white nodules are scattered throughout the lower lobe.

12. Meltzer, Sara: Neuroblastoma Occurring in Adults, *Canad. M. J.* 16: 647 (June) 1926.

In 1910, J. Homer Wright¹⁰ called attention to a group of tumors the nature of which has hitherto escaped general recognition. The essential cells of the tumor are considered to be more or less undifferentiated nerve cells or neurocytes or neuroblasts, and hence the names neurocytoma and neuroblastoma. They are considered to be neurocytes or neuroblasts for the following reasons:

1. The cells, at least in places, are associated with delicate fibrils, often of considerable length, which do not stain like neuroglia, collagen or fibroglia fibrils by Mallory's methods, and which are like the fibrils occurring in the "anlage" of the sympathetic nervous system.

2. The cells associated with these fibrils have the same morphology as the cells from which the sympathetic nervous system and the medulla of the adrenal develop, and which are regarded by embryologists as arising from migrated primitive nerve cells.

The fibrils may be arranged parallel to one another in bundles which are intimately associated with masses of the cells, as are the fibrils with the neurocytes in the "anlage" of the adrenal of a human fetus in the fourth or fifth month.

The tumors reported were found in the liver, lungs, adrenals, calvarium, brain and retroperitoneal tissue.

The occurrence of these tumors in such a variety of situations is accounted for not only by metastasis but also by the generally accepted teaching that undifferentiated nerve cells migrate from the embryonic central nervous system to form the nerves and ganglia as well as the sympathetic system.

Moreover, it seems reasonable to believe that certain other small cell tumors without the characteristic fibrils, occurring in various situations, are also of this nature.

Lederer¹¹ reported a case in 1926, which he classified as a neuroblastoma of the suprarenal gland. R. S., a girl, aged 4½ years, two months before admission had a swelling which appeared on the left side of the head and the left eye became prominent. At autopsy, a tumor involving the left suprarenal was found.

The cranial bones were involved. Tumors in this region "were of an osteoclastic nature as evidenced by a cellular invasion and osseous absorption."

In discussing the case he said:

In the primary tumor the ganglion cells were in parts of the tumor, being present in groups, or scattered singly among the spindle cells. In the metastases, however, after careful and prolonged search, no ganglion cells could be discovered. This corresponds to the observations of most authors that these tumors metastasize only by virtue of the undifferentiated cells. The absence of differentiated cells in the metastases is the chief reason for both

10. Wright, Homer, J.: *Neurocytoma or Neuroblastoma: A Kind of Tumor Not Generally Recognized*, J. Exper. Med. July, 1910, vol. 12.

11. Lederer, Max: *Neuroblastoma of the Adrenal Gland (Hutchinson Type)*: Report of a Case, J. Cancer Research, 1926, vol. 10.

fibrils or fibrous tissue. Comparing these neoplastic cells with the normal small round mono-nucleated cell, they were larger and more irregular in size and shape. The neoplasm was extremely vascular.

He summarized his observations and his study of the literature as follows:

As regards the occurrence of these tumors in such varied positions, this can be explained by the fact that the primitive nerve cells wander out from the embryonic central nervous system to form the sympathetic nervous system, and consequently tumors of this type may be found almost anywhere.

Finally, neuroblastoma may not be as rare as they were originally considered to be, as many which were or are diagnosed as sarcomata are really of nervous tissue. Of the two types neuroblastoma and ganglio-neuroma, the latter is the rarer of the two.

Of late years the interpretation of tumors of the nervous system has undergone many changes. For example, some years ago, the present case would have been classified as a sarcoma of the small round-cell type, but now it is recognized that neoplasms of the nervous system may be composed of the developing cells of the various parts of the nervous system. The neuroglia, or its various modifications may form tumors; as can also ganglion cells with nerve fibers, or the comparatively undifferentiated cell, which is the antecedent of these tissues. Thus we find tumors composed of cells which are the forbears of the sympathetic system, the chromaffin system, and the ganglion cells or neuroglial cells.

In the formation of the nervous system the epiblastic cells which line the medullary groove can develop into nervous elements or the supporting glial tissue. Nerve fibers may grow out from this central region and form the peripheral nervous system, or on the other hand neuro-epithelial cells may wander into the body and organs, and in relation to these organs give rise to the elements composing the sympathetic system.

In 1914, H. R. Wahl¹⁴ reviewed the subject of neuroblastoma. He reported:

It is becoming recognized, especially in the last four or five years, that the most highly differentiated tissue of the body—the nerve tissue—may and does frequently undergo blastomatous change. True nerve tumors, i. e., growths consisting of specific nerve elements, may occur in any part of the nervous structure, but by far the greater number of them have their origin in the sympathetic system. These tumors may be either benign or malignant.

In his summary and conclusion, he stated:

Nerve tissue may give rise to new growths, which are properly called neuroblastoma.

Neuroblastomata are manifestations of a pathologic condition more or less localized or diffused in the whole or part of the nervous system. If localized to one focus, as is usually the case, the result is a solitary nerve tumor (ganglioneuroma); if generalized, multiple tumors result.

14. Wahl, H. R.: Neuroblastoma, with a Study of a Case Illustrating the Three Types That Arise from the Sympathetic System, *J. M. Research*, 1914, June, vol. 30.

Summary: Neuroblastoma is a tumor almost confined to infancy, and early childhood. Both of the cases recorded in this paper occurred in adults.

In the microscopic picture one feature common to both tumors is the absence of "rosettes." We know that in the development of the sympathetic system the cells are frequently found arranged in rosette form. In the fully developed adrenal medulla these do not occur. This raises the possibility of some relationship between the age of the patient, and the finding of "rosettes" in the microscopic structure.

As the tumor is derived from the primitive nerve cell or neuroblast it may occur in any situation where such cells are encountered. It is, however, confined almost entirely to the sympathetic nervous system, and occurs most frequently in the medulla of the adrenal which itself is derived from that system.

It was pointed out some years ago by Frew that the site of the metastases depends on whether they are derived from the right or left adrenal. Thus if the primary tumor occurs in the left adrenal metastases will appear most frequently in the bones, especially the calvarium, but also in the liver and other organs, thus giving the first clinical variety. If the tumor is derived from the right adrenal, secondaries occur in the upper surface of the liver, the lung, and more rarely in the calvarium, and these fall into the second clinical group. We see that secondary growths occur most frequently in the skull, liver, and lungs, but they also occur in any of the bones, the sternum, vertebrae, ribs, and long bones: in the opposite adrenal, in the kidneys and even in the skin.

Apart from its position there is nothing characteristic in the gross appearances of a neuroblastoma. Microscopic, however, it possesses certain definite characteristics and a typical case can be recognized without difficulty.

Flemming and Davidson¹³ reported a case in a boy, aged 4 years. The autopsy observations were:

The whole of the subcutaneous tissue of the scalp was replaced by a red fleshy mass of tumor growth. This growth covered the whole of the frontal, parietal, occipital, sphenoidal and part of each temporal bone on either side. It was dark red in color and had the appearance and consistency of muscle. Over the parietal bone the neoplastic mass was 1.5 cm. in thickness.

On section of the skull, the neoplastic growth was seen to penetrate the bone, so that most of the extradural space was occupied by a mass of malignant growth. There was very marked invasion of the internal surface of the frontal bone.

Suprarenal Glands. The left suprarenal was replaced by a large homogeneous, dark red, comparatively soft mass, 6 by 5.5 cm. in size.

Long Bones. Both those of the upper and lower limbs were definitely involved. The marrow was almost entirely replaced by tumor growth which invaded the bone, making it extremely friable and thin.

Microscopic Appearances—Primary Neoplasm. The tumor was composed of small cells which were either roundish or elongated in shape. There was very little cytoplasm present, the most of the cell being occupied by a nucleus which in many cases was hyperchromatic. In certain areas these cells tended to assume a "rosette" or circular formation. Interspersed among the cells was a meshwork of fine fibrils which did not stain with the specific stain for glial

13. Fleming, Robert A., and Davidson, James: *A Case of Neuroblastoma (Neurocytoma)*, Tr. Medico-Chir. Soc., Edinburgh. 1924-1925, pp. 142-151.

Whether this is a neurocytoma or neuroblastoma of the variety described by J. Homer Wright or whether it is a metastatic carcinoma with the lung as the site of the primary lesion, cannot be definitely stated at this time.

Neoplasms of the peripheral nerves associated with evidence of pulmonary lesions should certainly direct attention to the lung as a factor before operative intervention is resorted to.

The recognition that true tumors of the nerve, either benign or malignant, do occur in any part of the nervous system should be more generally appreciated.

ENCAPSULATED TUMOR OF THE SPINAL ACCESSORY NERVE

Solitary neoplasms of cranial nerves must be considered when differentiating masses in the neck. This single point is my reason for adding the third case to this presentation.

CASE 3.—Mrs. G. L., aged 53, was referred by Dr. I. I. Lemann because of the presence of a swelling on the right side of her neck. This swelling had been noticed only two months before she came under observation. There was a history that the mass increased and diminished in size. She complained that the mouth was dry and that recently there had been a small amount of saliva. Pain was not associated with the mass.

This patient had been under Dr. Lemann's care because of hypertension.

Tonsillectomy had been performed by Dr. R. C. Lynch one and one-half years before the present examination. Following the operation, there was a secondary hemorrhage which was controlled by sutures.

Examination.—She was examined on April 29, 1927. There was swelling on the right side of the neck which extended down to the upper level of the thyroid cartilage. The mass lifted up the sternomastoid muscle and seemed to extend upward to the tip of the mastoid. The skin over it was neither red nor glossy. Pulsation was not noted in the mass. There was a pulsation below the level of the mass, and this pulsation seemed to extend upward from the junction of the middle of the upper third of the clavicle and reached the sternomastoid about its middle posteriorly. A pulsation was noted in front of the mass, and this corresponded to the facial artery.

No palpable mass was found about the ascending ramus of the mandible on the right side. When the patient opened and closed her mouth, the condyle immediately under the skin could be palpated. The glands in the digastric triangle on both sides were palpable. There was a mass, the lower limit of which corresponded to the upper limit of the thyroid cartilage, which could be palpated as high, I believe, as the tip of the mastoid. The mass was not adherent to the muscles and could be moved laterally. It was not nodular, but seemed to be smooth. No pulsation was imparted to the finger. I could get a lateral range of motion of about 1 inch. The floor of the mouth did not show bulging, and with the finger in the mouth I could feel a mass lying immediately on top of what I believed to be the internal carotid artery. The mass did not cause any bulging of the posterior pharyngeal wall. There was no bruit over the mass.

The diagnosis was probable tumor of the carotid body.

Owing to the extensive variation in the degree of differentiation of the cellular and fibrillar structures in the undifferentiated type of nerve tumors different portions of a malignant neuroblastoma may differ widely in their appearance.

The possibility that this case represents metastatic carcinomas with the lung as the site of the primary growth cannot be overlooked.

Reference to Barron's excellent work on carcinoma of the lung is convincing. He stated:

The metastases from lung carcinomas are frequent and numerous. According to Adler, the principal metastases in his collection of 374 cases were to these organs: (1) lymph nodes, 117; (2) liver, 103; (3) lungs, 66; (4) kidneys, 58; (5) suprarenals, 38; (6) brain, 28 (dura mater, 10), and (7) bones (vertebrae, 5).

Briese, in his series of sixty cases, found metastases absent in only four cases. Of the twenty-one organs and tissues listed in the order of frequency, the principal ones involved were: (1) regional lymph nodes, 43; (2) liver, 25; (3) pleura, 17; (4) kidney, 17; (7) lungs, 11; (8) brain, 11; (9) bones, 9; (12) ovary, 7; (13) suprarenals, 6 and (17) dura, 3.

It is true that none of his collected cases present evidence of metastases to peripheral nerves, but there is evidence of metastases to the brain and spinal cord.

The other organs involved in our case are frequently involved in cases cited (liver and suprarenals).

Brunn stated:¹⁵

Metastases occurred in 85 per cent of the cases. Many of the initial symptoms were due to metastatic involvement. These occur relatively early and may be the condition that brings the patient to the doctor. A great many of the clinical diagnoses were made on metastatic involvement, mainly cerebral or bone involvement. The brain was involved in 12 per cent of the cases, the liver in 30 per cent, and the kidneys in 20 per cent. Two striking features in the occurrence of metastases are that the heart was involved in 21 per cent of the cases and the suprarenals in 14 per cent in a study of 626 case reports.

Lanford stated specifically that all of the growths may be considered metastatic carcinoma, except those of the nerve.

We know this patient had evidence of lung involvement before the tumor of the nerve appeared. Reference to his history shows that he was treated for tuberculosis long before he came under our observation. This is a common error.

Summary.—My second case illustrates a type of malignant epithelial neoplasm which not only recurs in the original nerve, but which may involve other peripheral nerves.

15. Brunn, Harold: Primary Carcinoma of the Lung. *Arch. Surg.* 12:405 (Jan.) 1926.

running across it, giving the appearance of a myxomatous tumor. The cord previously mentioned looked like a nerve bundle.

Progress Notes.—Convalescence was uneventful except for slight parotitis. The wound healed primarily.

The laboratory examination (July 13) showed the specimen to be an irregular oval mass of tissue, measuring about 5 cm. in diameter, with a small projection about 0.5 cm. thick and apparently made up of a number of individual fibrils suggesting a nerve. The outer surface varied in color from a red to a yellow tinge, and the entire mass was pseudo-encapsulated. It was soft, but uniform. On section, it offered little resistance to the knife and presented a cut surface that varied from a light pearly gray to a pinkish tinge and was divided into irregular lobules by a connective tissue of increased consistency. The blood vessels were not prominent. Cellular neoplasm of undetermined type was diagnosed.

Microscopic examination showed that the specimen was made up of a number of cells occurring in irregular masses which were differentiating into nerve tissue. Some of the cells showed large vesicular nuclei, and in others, mitotic figures were present. The older cells showed a relatively well defined nuclei and a cytoplasm scanty for the most part and divided into innumerable little fibrils which were anastomosing with similar fibrils from other cells. The histology suggested glioma, whereas other areas suggested a more cellular form of neoplasm.

The diagnosis was neurocytoma (Lanford).

August 8: The examination following operation showed that the wound was entirely healed. There was no discharge. There was still some enlargement of the right side of the neck, and the skin was infiltrated. There were enlarged glands in the supraclavicular region. There was atrophy of the trapezius, supraspinous and infraspinous muscles of the right side.

The patient did not voluntarily completely extend the right elbow. The right shoulder was lower than the left. She volunteered the statement that she was unable to get her arm up to comb her hair.

August 10: She returned to the hospital, where 1,950 mg. hours of radium treatment was applied to the right side of the neck.

August 27: Atrophy of the muscles about the right shoulder was noted.

November 21: The right shoulder was much lower than the left. The clavicle was prominent, particularly near the acromioclavicular joint. There was a definite depression on either side of the clavicle at the outer end. Marked atrophy of the trapezius and supraspinous and infraspinous muscles was noted. Abduction of the arm was painful, and atrophy was more prominent when the arm was abducted.

Voluntary extension of the elbow was limited to about 150 degrees. Passive extension beyond that point was painful.

There was no limitation of rotation of the head. When the head was inclined to the left side, there was some discomfort as of stretching. No mass was palpable in the mouth.

The operative scar was smooth and freely movable. There was no palpable mass in the region of the previous tumor.

This tumor was solitary, encapsulated and developed along the course of one of the cranial nerves. For these reasons, it seemed to fall in the same class as neurinoma and acoustic neuroma. This classification is correct if the tumor arose from the sheath of Schwann, according to Verocay and Cushing.

Lanford's description would seem to place it in this category.

From my examination, I had the impression that it was a tumor of the carotid body for the following reasons:

There was a discrete, smooth, nonpulsating mass which had lateral mobility, but none in the long axis of the body. It was not adherent to the underlying structures. There was nothing which in any way would lead one to suspect aneurysm because of the absence of expansile pulsation and also because of the absence of bruit.

Primary carcinoma of the lymph glands of the neck is so rare as to rule it out ordinarily; more than that, the lack of fixation, the fact that the mass was discrete and that there were no similar masses seemed to eliminate carcinoma.

The blood dyscrasia seemed to be ruled out by the observations of Dr. Lemann. Cysts in the neck, branchial, thyroglossal, ranula were not usually found at this age. Aberrant thyroid must be considered, but the smooth, rounded contour seemed to eliminate that in my mind. Syphilis and tuberculosis seemed to rule themselves out on many grounds.

The diagnosis of tumor of the carotid body was made both by elimination and by the manifestations present.

The operation was not performed until July 13, 1927.

The preoperative diagnosis was undetermined, but several conditions were considered among which were a tumor of the carotid body, branchiogenic carcinoma, aberrant thyroid and possibly a cured false aneurysm.

An incision was made from the tip of the mastoid process, 3 inches in length, extending along the anterior border of the sternomastoid. The sternomastoid was reflected outward and the carotid vessels and jugular were exposed and retracted medially. The sternomastoid was lifted up, and the tumor could be palpated under it as far as the angle of the jaw.

The parotid gland was exposed at the upper angle of the incision. In order to have better exposure of the tumor, a second incision was made, beginning at the upper limit of the original and extending obliquely downward and backward along the mastoid process for about 2 inches.

The sternomastoid was cut across and reflected. This permitted us to obtain a free exposure of the mass. A tumor mass, about $1\frac{1}{2}$ inches long and $\frac{3}{4}$ of an inch wide was seen to occupy a position immediately lateral to the great vessels of the neck. The upper limit of the mass was continuous with a small "cord," the lower limit was continuous with a similar "cord" which extended down a short distance paralleling the vessels. The tumor itself, between the upper and lower structure, with which it fused gave the appearance of a punching bag suspended from a ceiling and held fast by an attached cord to the floor. The fibers of the cord above and below spread out over the bulbous enlargement like a fan. The upper portion of the cord could be followed upward under the mandible.

When an attempt was made to dissect the tumor away from this fanlike projection over its surface, we found that this was impossible.

The tumor was excised well above the upper limit of the bulbous enlargement and well below the bulbous enlargement. While we were removing the mass, that portion which had previously been described as being thin-walled ruptured, and a dark-yellowish material (which did not give the impression that it was gaseous) was spilled in the field. The mass was removed and turned over to the pathologist. All bleeding points were clamped and ligated, muscle planes approximated and skin closed. A gross section of the tissue showed a cavity with smooth, thick walls and many blood vessels

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Penfield¹⁶ denies that this group arises from this source. He stated:

The fibers produced in these neoplasms show that the type cell bears no relation to neuroglia nor to the ectodermal sheath of Schwann cells.

Mallory (1920) in a careful histological study of the type cell of the so-called dural endothelioma suggested that the fibroblast was the type cell of the nerve sheath tumor as well as of the "endothelioma." He therefore proposed the name "peri-neurial fibroblastoma," assuming an origin from the connective tissue which surrounds the nerve. Inasmuch as we have found that the fibers in these tumors are not neuroglial and not nervous in nature but represent a particular form of collagen it is obvious that we must confirm Mallory's opinion provided the neurofibromata be excluded from the group.

The perineurial fibroblastoma must be considered to arise from the peri-neurial or endoneurial connective tissues which invests nerve fasciculi and fibers.

CONCLUSIONS

1. It may be presumptuous to attempt to classify this tumor in accordance with Verocay, Cushing and Lanford, in opposition to Mallory and Penfield; yet in view of the fact that I believe that the sheath of Schwann is ectodermal in origin and the fact that Lanford found cells which suggest "differentiation into nerve tissue," I believe that it is justifiable to consider this an epithelial neoplasm.

Future investigation may change the designation.

The essential points for us as surgeons are:

2. To recognize that solitary tumors of the nerve occurring in or on a peripheral or cranial nerve occur more frequently than we have accustomed ourselves to believe.

3. These tumors must be considered when masses in the neck are differentiated.

4. This tumor of the spinal accessory nerve was solitary. Up to the present time, the patient is comfortable, without any evidence of further trouble.

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16. Penfield, Wilder: The Encapsulated Tumors of the Nervous System. *Surg. Gynec. Obst.* 47:178 (Aug.) 1927.

cause the injury that knife incision of the parenchyma would cause. Hemorrhage is avoided both during and after operation. Collective statistics on nephrolithotomy indicate that hemorrhage is usually frequent. At the International Urological Congress in Rome in 1924, collective statistics were given in 686 cases of nephrotomy; serious bleeding occurred in 85 (13.5 per cent) and 22 of the patients died.

If nephrectomy is indicated in cases of malignant tumor, tuberculosis or pyonephrosis, Rovsing begins by doubly tying the ureter with silk a few centimeters below the pelvis, and with cautery sears through the ureter slowly and cauterizes the mucous membrane in the lumen. Next, the kidney is isolated, care being taken that the capsule is not ruptured. The vessels are ligated with strong catgut and the kidney delivered through the wound. Then an incision 2 cm. long is made through the skin and fascia in the iliac fossa. A blunt perforation in the muscles and peritoneum is made and the peripheral stump of the ureter is drawn through and fixed to the skin. This guards against infection from the ureter, and in tuberculosis any subsequent tubercle of the ureter and bladder can be treated by the injection of a solution of carbolic acid.

Rovsing regards nephrectomy in polycystic kidney as inexcusable, even though some patients survive the operation. The disease is always bilateral and so little functioning renal tissue remains that uremia is not infrequently a sequel to the removal of one of the kidneys. It is essential to protect and set free as much as possible of the remaining kidney which is compressed by the tension of the cysts. This is done by multiple puncture of the exposed kidney which reduces it to normal size. The kidney is replaced and the wound closed around a drain. Oozing of urine or a chronic urinary fistula never occurs. Relapses are rare and renal function improves immediately after this type of conservative surgical procedure.

Rovsing uses a simple method of nephropexy which has the advantage over other methods of fixing the kidney securely in an absolutely normal anatomic position without injury, without leaving foreign bodies and without fixing the kidney to osseous structures. An angular incision is made, starting externally to the erector spinae muscle at the level of the tenth rib, passing perpendicularly down to midway between the twelfth rib and the iliac crest, and from there going forward for 10 cm. The kidney is drawn out through this incision, after being carefully loosened from its adhesions to the peritoneum and fat capsule. Retracted strands of fascia along the ureter are severed or loosened with a blunt instrument, as they tend to draw the kidney down again and cause pain. The membrane is incised longitudinally from the upper end to the juncture between the third and fourth quarters of the kidney, and from the ends of this incision, transverse ones are made out to the

A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.

LOS ANGELES

E. STARR JUDD, M.D.

ROCHESTER, MINN.

LINWOOD D. KEYSER, M.D.

ROANOKE, VA.

GORDON S. FOULDS, M.D.

TORONTO

JEAN VERBRUGGE, M.D.

ANTWERP, BELGIUM

AND

ADOLPH A. KUTZMANN, M.D.

LOS ANGELES

KIDNEY

Surgical Technic.—Rovsing¹ discusses his technic in operations on the kidney. The conditions most conducive to good results are the position of the patient and the incision which will give free access to the swollen, friable and adherent kidney. According to his procedure, the patient is placed on his back, in such a position that the edge of the table coincides with the free border of the erector spinae muscle, from which the lumbar region is readily accessible for the incision that begins midway between the twelfth rib and the iliac crest and continues forward to the border of the rectus muscle in cases of large tumor. In cases in which the ureter is to be exposed, the incision passes around the anterior superior spine of the ilium obliquely down toward the symphysis pubis. Through this incision, the hand may be introduced into the retroperitoneal space, and the kidney carefully and definitely isolated from its surroundings, thus bringing it uninjured outside the wound. This is important in ordinary suppurative processes, and in cases of tuberculosis and malignant tumors it is absolutely necessary in order to insure a good result.

In case a single stone lies free in an aseptic renal pelvis, Rovsing does not remove it through an incision in the pelvis. As a rule, he performs nephrolithotomy in the following manner: The stone is held between the thumb and index finger of the left hand, while an incision is made with a small knife in the capsule on the convex side of the kidney over the site of the stone. A forceps is then forced through the renal tissue on to the stone, dilating the opening so that a stone forceps may be inserted and the stone removed. This method does not

1. Rovsing, N. T.: My Technic in Operations on Kidney, Practitioner 116: 164, 1927.

children. Mathé employs the silver wire method in opening the parenchyma of the kidney, and during the procedure he clamps the pedicle in order to lessen hemorrhage. He uses a double layer of mattress sutures to close the kidney. Fat is included in these sutures to prevent postoperative hemorrhage.

Phlebitis occurred in 2.8 per cent of Mathé's cases. It usually occurred in the internal saphenous vein. Treatment consisted of rest, compresses of hot boric acid and elevation of the affected member. Quinine, given either by mouth or intravenously, seemed to hasten recovery.

In thirty-two cases of nephrectomy for tuberculosis, the wound healed in the average time of ten weeks, and in nephrectomy for pyonephrosis, the average was three weeks.

Mathé pays careful attention to cardiac complications; in most of his cases the heart is examined by a competent internist before operation. Some patients are put on a digitalis regimen prior to surgical intervention. Mathé gives 15 drops of a digitalis product hypodermically every four hours after the operation until the pulse reaches 70. Although the peritoneum was opened on a number of occasions, symptoms of peritonitis did not develop. Usually, operations on the kidney can be performed extraperitoneally. In dissecting out large adherent tumors care should be taken not to injure the pleura. In case the pleura is injured, low-grade pleurisy develops, which usually clears up in a week or two.

In 50 cases in which operation was performed between 1906 and 1916, a period before complete urologic examinations were made, the mortality rate was 6 per cent. Between 1916 and 1926, the mortality was 2.04 per cent in 320 cases. A careful estimation of the renal function and a study of the working power of the opposite kidney allows elimination of cases with a poor risk.

Hinman, in discussing Mathé's paper, did not feel so confident about the safety of leaving clamps in place following nephrectomy, as Mathé has done in a number of cases. Hinman calls attention to a rather high percentage of fatal postoperative hemorrhages following release of the clamps, and he expresses the opinion that the clamps should not be left on except in extreme emergency. He has not left clamps on during the last ten years. He always carries out hypodermoclysis during the operation, so as to supply plenty of fluids to the patient before he recovers from the anesthetic. Hinman believes that a large proportion of failures in conservative as well as radical operations on the kidney are due to secondary infections. These infections are produced or made more serious by rough and prolonged operation. Dispatch at the time of operation is one of the greatest assets of successful renal surgical procedures.

sides. The membrane is then separated with the help of a flat sound, so that it looks like two folding doors or wings out to the sides. A strong piece of catgut is passed in and out through the portion of the membrane attached to the lower end of the kidney with a special needle curved on the flat plane. The ends of the catgut suture are next threaded through large curved needles and passed out through muscles and fascia to each side of the upper end of the lumbar incision. They are tightened until the kidney in the loop of catgut is drawn up into the exact normal position, and are tied over the fascia at the level of the tenth rib. The lumbar wound is sutured in four stages, the fascia and the skin with metal, and the muscle with catgut. After a period of from ten to fourteen days, the kidney is fixed in the normal position by the two wings of membrane. Rovsing has performed this operation about 300 times and considers it almost ideal. Pain entirely disappears, and in only 10 per cent of his cases has it partially returned.

Rovsing first performed nephrolysis in 1892, in a case of medical nephritis of the type which is now called nephrosis. Since then he has performed operations in at least 100 cases of nephritis that had been refractory to medical treatment, with an operative mortality of 4 per cent.

In cases of painful horseshoe kidneys without infection or other complications which would necessitate removal of one kidney, but in which it is simply a question of preserving all the renal tissue, Rovsing performs laparotomy through an incision in the rectus muscle, and exposes the isthmus by an incision in the posterior sheet of the peritoneum. The tissue of the isthmus is slowly crushed through with a powerful angiotribe until only the capsule persists. The angiotribe is removed and replaced by two narrow clamping forceps between which the capsule is cut through. The capsule is sewed close to the renal tissue with a continuous catgut suture, the forceps are taken off, and the liberated kidneys immediately retract into their respective beds. The two peritoneal wounds are carefully sutured and the abdominal incision closed.

Surgical Complications.—Mathé² reviews 370 cases of disease of the kidney in which operation had been performed in St. Mary's Hospital, San Francisco. The most common complications were shock, hemorrhage, cardiac lesions, phlebitis and embolus.

Surgical shock or exhaustion occurred most frequently in cases in which a considerable amount of blood had been lost after the removal of a large kidney. All bleeding points should be securely ligated during the operation. Loss of blood should be particularly guarded against in

2. Mathé, C. P.: *Renal Surgery: Its Pitfalls and Complications*. California & West. Med. 28:57, 1928.

Nephropexy.—Petit,⁶ who studied the late results in a series of cases in which nephropexy was performed during the last twelve years, concludes that this operation gives more lasting and better results in cases in which there is renal retention or persistent oliguria. The results are less satisfactory in cases in which nephropexy is performed because of pain in the region of the kidney without other urinary distress.

If patients are in pain because of a movable kidney, and are nervous and dyspeptic, signs of renal retention should always be investigated. This should be accomplished by means of ureteral catheterization.

If orthopedic or medical treatment does not relieve the patient, nephropexy should be performed because such kidneys usually contain fibrous or perinephritic lesions which diminish their functional value and predispose them to infection.

Foreign Bodies.—Brattstrom⁷ reports a case in which two grass straws covered with concretions were found in the renal pelvis. The straws had probably been introduced through the urethra to the bladder and had found their way into the ureteral orifices and later the kidney. Nephrectomy was performed.

Tuberculosis.—Kidd⁸ states that tuberculosis of the urogenital tract is a disease of adolescence, as common in males as in females, and induced by the stresses of puberty, work, marriage and parenthood. Clinical experience suggests that the human and bovine type of *Bacillus tuberculosis* produce two different types of disease. The first runs a rapid course and proves fatal in two or three years, a type which may be due to an infection with the human strain of the bacillus. The second runs a slow course of from ten to twenty years, in which the prognosis is excellent after surgical intervention, and in which the bovine type of bacillus may be concerned.

The bacillus is absorbed into the blood stream and may infect the kidney, seminal vesicle or testicle primarily, and no other organ of the body. In most cases, tuberculosis of the kidney appears as a unilateral blood borne infection. In women, the disease always starts in the substance of a kidney and extends into its pelvis, producing pyuria and increased frequency of urination. In men, the disease may start primarily in the testicle, extending along the lymphatics of the vas to the vesicle, prostate and base of the bladder, or it may start in both the testicle and the kidney.

6. Petit: Les résultats lointains de la néphropexie, *Presse méd.* 2:1365, 1927.

7. Brattstrom, Erik: Unusual Case of Foreign Body in Kidney, *Acta chir. Scandinav.* 62:56, 1927.

8. Kidd, Frank: Treatment of Tuberculosis of Kidney, *Practitioner* 118:150, 1927.

Manson states that he agrees with Hinman concerning the leaving of clamps on the renal pedicle. If the clamps are left on, they should be removed with the greatest care by loosening a notch or two at a time for one or two days before complete removal. Too rapid or rough removal of a clamp may open up a vessel and start bleeding. Manson believes that the perirenal fat is frequently involved with the tuberculous kidneys, and should usually be removed also. He does not remove the ureter, but sutures it to the skin at the lower angle of the wound; in this way the wound does not break down.

Renal Decapsulation.—Molina³ reports several cases of mercuric poisoning. One case was that of a young woman who had absorbed 2 Gm. of mercuric chloride. Various forms of medical treatment did not prevent the appearance of anuria. Bilateral decapsulation of the kidneys was performed thirty-six hours after the onset of anuria. The patient gradually recovered and passed a normal amount of urine. She was completely cured nineteen days after surgical intervention.

In comparing the surgical with the medical results, Molina agrees with Pousson, Legueu and Tisserand, that in cases of toxic nephritis, it is absolutely necessary to perform an operation as soon as anuria sets in. The operation, which should be performed quickly and without shock to the patient, does not cause disturbance of the renal function later.

[Ed. Note.—Quinby⁴ reports a similar case in which decapsulation was performed for acute tubular nephritis from mercuric chloride poisoning. This patient was not benefited by the operation, and died five days after the onset.]

Contusions.—Klenka⁵ reports three cases of wounds of the kidney. The first case was one of traumatic rupture of the kidney. Cure followed suture of the renal tear. In the second case, the upper third of the kidney had been torn away. Hematuria did not set in until seven days later. In this case, it was necessary to perform nephrectomy. In the third case (rupture of the kidney), the patient refused operation. For two months hematuria was intermittent and accompanied by fever. Nephrotomy was finally performed and a large perinephritic hematoma was found. The kidney was markedly congested but an outstanding tear was not found. Klenka believes that numerous fine lesions were present, but invisible macroscopically. The pressure of the hematoma against the kidney probably stopped the bleeding.

3. Molina, A. C.: Décapsulation du rein pour néphrite aiguë par intoxication mercurielle: un cas de guérison. *J. de chir.* 29:496, 1927.

4. Quinby, W. C.: A Note on the Results of Decapsulation of the Kidney for Various Forms of Nephritis. *J. Urol.* 13:321, 1925.

5. Klenka, Z.: Trois cas de plaies contuses du rein. *Bratisl. lekár. listy.* 6: 315, 1927.

1920, and details were obtained concerning 317. One hundred ninety-five of the patients (61.5 per cent) were cured; 28 (8.7 per cent) were not cured and 94 (29.9 per cent) died subsequent to the operation. One hundred and four of 125 patients operated on more than ten years previously were traced; 44 were dead; 58 (55.7 per cent) were cured and remained well.

Judd and Scholl report 863 nephrectomies: 611 patients were traced; 58 per cent were cured, and 31 per cent had died.

Wildbolz employs injections of tuberculin in many of his cases. The process of cure in these cases had been more certain and more rapid than in those in which tuberculin was not used. He believes that small doses of tuberculin are efficient. Small doses stimulate resistance, but large doses overwhelm and break down resistance. Kidd employs Koch's new tuberculin. Tuberculin should not be given until six weeks after an operation, and doses should be started with 0.00001 mg. If at the end of two years there are still traces of pus and bacilli in the urine, injections of tuberculin should be continued.

Thomson-Walker⁹ states that renal tuberculosis is a disease of young adults, occurring most frequently between the ages of 20 and 40. It is rare in children, and is often bilateral in the early stages. In adults, chronic renal tuberculosis is unilateral in about 80 per cent of cases in the early stage.

Primary tuberculosis of the kidney rarely exists. A primary focus is always present elsewhere in the body, although it may not be discovered clinically. Coincident lesions were found by Braasch in 71 per cent of 346 surgical cases; they were noted by Persson in 50 per cent. In Thomson-Walker's cases, tuberculous lesions were noted elsewhere in the body in 40 per cent. In order of frequency, these extrarenal lesions are in the bones and joints and in the genital tract in the male. In Thomson-Walker's cases, there were tuberculous lesions in the epididymis in 23 per cent, in the prostate in 15 per cent and in the seminal vesicles in 7 per cent.

Miliary tuberculosis is usually an acute condition in which both kidneys are studded with tubercles. It is a part of general tuberculosis and is not of surgical interest.

Usually the first change takes place at the apex of a pyramid. Ulceration spreads outward toward the base of the pyramid, and a cavity communicating with the calix forms. Beyond this, there is a zone of inflammation which may show tubercles. Outward from this zone, isolated tubercles are scattered through the renal tissue. On the surface of the kidney, groups of tubercles are seen in areas corresponding to the subjacent tuberculous pyramids.

9. Thomson-Walker, Sir John: Tuberculosis of the Kidney, *Brit. M. J.* 2: 625, 1927.

The most deceptive feature of tuberculosis of the kidney is the absence of pain in both kidneys until the later stages of the disease, and it is difficult to realize that one of the kidneys may be destroyed by the tuberculous process. The healthy kidney may ache at times because it is heavy, having increased to double its size in order to carry on the work of both kidneys.

In the more acute types, the onset of symptoms is an attack of profuse hematuria, which may be repeated once or twice. Pyuria is one of the most constant signs, but in chronic cases there are periods in which the pus disappears from the urine entirely, owing to ureteral obstruction. The general condition of the patient is usually satisfactory for the first year or two except in acute cases. There is no anemia or wasting, and there is no fever as long as the infection remains unmixed; later secondary infection from colon bacilli may occur which will induce fever.

In cases in which it is impossible to see the ureteral orifices, Kidd makes a small abdominal incision just below the umbilicus. Through this he inserts a gloved finger and palpates the ureters on each side as they cross the brim of the pelvis. If one ureter is thick and the other normal, and if the blood urea is within normal limits, he removes the kidney on the side of the thickened ureter.

Tuberculosis of the kidney inevitably leads to death after years of pain and misery unless the kidney is removed by operation. Early diagnosis, followed by nephrectomy, results in complete cure in at least 60 per cent of the patients so treated. In expert hands, due to the precision and accuracy of urologic diagnosis and surgical procedures, the mortality following operation should be less than 2 per cent. In 65 consecutive cases there were no deaths; the condition of 38 patients was observed until they were completely cured, in a number of instances from ten to fourteen years after operation. These data indicate that between 50 and 60 per cent of the patients should obtain permanent cure. Healing occurred by first intention in 36 of the 65 operations. Kidd removes not only the kidney, but the fatty capsule intact.

Legueu and Chevassu report 708 cases in which nephrectomy was performed for tuberculosis. Half of the patients were completely cured, one-fourth were improved, and one-fourth died within ten years after operation. They reviewed 638 cases in which the treatment was nonsurgical; 356 patients (51 per cent) died, mostly within from two to five years; 282 were alive, 22 more than ten years after the diagnosis had been made. They review data on 184 cases in which tuberculin was used; 51 of the patients were believed to have been cured.

Wildbolz performed an operation on 445 patients for renal tuberculosis; 11 (2.4 per cent) died within six weeks of heart lesions or embolism. Four hundred sixteen patients had been operated on before

In most cases the wound is closed without drainage. Drainage may be necessary on account of oozing or of infection of the perinephric tissues.

The operative mortality has fallen during the last twenty-five years. Recent statistics are satisfactory. In Thomson-Walker's 193 cases the mortality was 2.5 per cent. He was able to trace 111 of 188 surviving patients; 67 were well and without symptoms of urinary disease at periods of from one to twenty-two years after the operation; 25 were in good general health but still had symptoms. Of 19 patients who died after the operation, 11 (57.8 per cent) died during the first three years.

In none of Thomson-Walker's cases was cure obtained by tuberculin. Frequently symptoms were ameliorated and the general health improved for several years, but the tuberculous disease persisted. Tuberculosis of the kidney cannot be cured by exposure of the patient to sunlight; the temporary improvement that may take place encourages the patient to refuse operation or to postpone it. Heliotherapy is valuable after the operation; it is also useful in cases in which operation is contra-indicated.

In an inquiry among the physicians of Switzerland, Wildbolz found that of 316 patients suffering from renal tuberculosis and on whom operations were not performed, 31.3 per cent died within the first two years, and 27.2 per cent within from three to five years. More than half (58 per cent) died within the first five years, and only 20 per cent were alive after five years.

Fullerton¹⁰ recently investigated a series of 158 cases of tuberculosis of the bladder that had been observed for several years. There was definite evidence of renal involvement in 141.

Fullerton's most successful operations were removal of the kidney and of as much of the ureter as could be reached through the lumbar wound. He did not find it necessary or desirable to dissect out the ureter. He believes that the removal of infected nodes surrounding the pedicle close to the spine is attended with risk. His present practice of dealing with the ureter at the point of section is to inject with a hypodermic syringe pure carbolic acid into the lumen for 2.5 cm. or more, before ligation and division of the ureter.

Nephrectomy was carried out in 73 of the cases; 6.8 per cent of the patients died as the result of operation. Fifty-five of the 68 surviving patients have been traced. Fifteen have died, 4 of them after long periods of complete relief. Forty-one patients not subjected to operation were traced; 26 (63 per cent) were dead.

10. Fullerton, Andrew: Statistics of Post-Operative Survival in Renal Tuberculosis, *Brit. M. J.* 2:630, 1927.

Tuberculous lesions of the kidney may be arrested as the result of one of two processes: (1) healing of the tuberculous lesions with disappearance of the *Bacillus tuberculosis* and replacement of the ulcer with a scar, and (2) exclusion of the tuberculous focus by a ring of fibrous tissue. This may occur in three ways: tuberculous hydro-nephrosis, massive caseous tuberculosis of the kidney and occlusion of an ulcerocavernous focus.

The discovery of the bacillus of tuberculosis is the final proof of urinary tuberculosis. The bacillus was found in the urine in 85 per cent of Persson's cases, in 70 per cent of Beer's and in 90 per cent of Wildbolz'. In 193 cases in which Thomson-Walker performed nephrectomy for renal tuberculosis, the bacillus was found in 155 (80.3 per cent).

The modern treatment of renal tuberculosis is nephrectomy in all cases if the other kidney is healthy and there is no definite contraindication. This treatment is based on three postulates of the surgical pathology of chronic renal tuberculosis: (1) tuberculosis of the kidney is a progressive disease, (2) tuberculosis of the kidney is unilateral in the early stage and bilateral in the late stage, and (3) removal of the tuberculous kidney usually prevents infection of the other kidney.

The immediate postoperative mortality of nephrectomy in bilateral renal tuberculosis varies from 66 to 80 per cent and the benefits gained in the few surviving cases have not been permanent. The procedure is justified only in exceptional cases.

Various methods of dealing with the tuberculous ureter have been described: (1) the ureter is cut across below the kidney, the end seared with cautery or with pure carbolic acid and dropped back into the retroperitoneal space, and pure carbolic acid is injected into the ureter; (2) the ureter is cut across below the kidney and the end is sutured to the skin in the lumbar wound, or is brought up to the surface inside a drainage tube and fixed there; (3) the kidney and ureter are removed through a lumbar iliac incision (nephro-ureterectomy), and (4) the kidney is removed by the lumbar incision and the ureter cut across. A second small incision is made in the inguinal region through which the ureter is removed.

The method that Thomson-Walker uses is to remove the ureter as far as the brim of the pelvis through the lumbar wound, sear it with the cautery or with pure carbolic acid, apply a ligature, and drop it into the retroperitoneal space. The patient is reexamined in six months, and if there is reason to believe that the disease is still active in the ureter and is infecting the bladder, extraperitoneal ureterectomy is performed through a median suprapubic incision. The cases in which ureterectomy is advisable are those in which there is stricture at the lower end of the ureter and dilatation of the duct. The proportion of cases in which this is required does not exceed 8 per cent.

immediate intervention is urged. Interruption of pregnancy does not stop the tuberculous process, and this procedure is increasingly dangerous in later months.

Pugh unhesitatingly recommends nephrectomy in cases of renal tuberculosis in pregnant women. He examined the records of thirteen cases in which nephrectomy was performed by others. In eight cases, uninterrupted pregnancy and delivery at full term resulted. In four cases, abortion had to be resorted to after the nephrectomy. The diagnosis in the remaining case was vague. Of three patients observed by Pugh, two came to full term following nephrectomy. The uterus of the third was emptied at the fourth month, the patient dying one month later. Apparently pregnant women stand the operation well, and it is not more serious than when attempted in the nongravid state.

Perirenal Hematoma.—Hübner¹⁴ states that clinical identification of perirenal hematoma was first described by Raye in 1839, and by Willis in 1841, and was called "apoplexia renum." Wunderlich later enhanced its clinical significance. There are many conjectures regarding the pathogenesis. There is no single explanation that covers all types of cases.

Perirenal bleeding does not always come from the kidney itself. Lâwen describes a hemorrhage from the iliac artery, which reached from the prostate to the diaphragm and encircled the kidney. A similar observation is made by Michaux following the spontaneous rupture of the epigastric artery. Not infrequently it is impossible to determine the source of the bleeding either by operation or necropsy; in one case, a massive hemorrhage was found in the renal region following scarlet fever. True perirenal bleeding is that coming from the kidney proper or the renal capsule, as well as those cases with blood between the fibrous capsule and surface of the kidney. These are more accurately designated as "perirenal hematomas," while massive hemorrhages are designated "retroperitoneal hematomas."

Chronic renal disorders have frequently been found associated with perirenal hematoma. The condition of the walls of the blood vessel and increased blood pressure have been thought to produce a hemorrhagic diathesis. Israel designates this as essential renal bleeding because of the absence of definite symptoms. Most authors, however, favor nephritis as the causative factor.

Hübner undertook some experimental work to determine the actual cause of the bleeding. He performed nephrotomy in some instances, and in others he clamped the renal pedicle, in periods varying from ten to thirty minutes, with the idea of creating a disturbance in the renal circulation. In most instances, definite subcapsular bleeding was noted.

14. Hübner, A.: Das Perirenale Hämatom. Experimentellar Beitrag zur Frage der Genese, Arch. f. klin. Chir. 145:338, 1927.

Statistics support the contention that, with our present knowledge, operation remains the most hopeful method of treatment. If performed early, before deep ulceration has taken place in the bladder, relief is often immediate.

[ED. NOTE.—Various reports recently have suggested the necessity of surgical procedures in unilateral renal tuberculosis. Joly¹¹ states that urologists are unanimous in advising early operation. Joly quotes Rafin as saying that 91 of 168 patients not operated on were dead, the majority within the first three years after the onset of symptoms. In all, about 90 per cent of patients with renal tuberculosis who are not operated on die from the disease. Even patients who survive are rarely free from symptoms. Clinical cures are so rare that they do not appreciably influence the statistics. Israel states that a nonoperative cure for renal tuberculosis does not exist. The infection may be well localized and of low virulence, or the patient may, by reason of chronicity and numerous foci of infection, have acquired a tolerance and resistance to the bacillus. Braasch believes that immunity develops with multiplicity of lesions. In most cases, the infection destroys the kidney, spreads locally, extends to the bladder, and often causes disease of the other kidney. Nephrectomy is the operation of choice. Conservative surgical procedures are not practical in cases of tuberculous kidneys, and at best afford only temporary relief.

The statistics of Kümmell¹² concerning the spread and extension of the disease noted at necropsy in cases in which operation had not been performed, suggest the course usually taken by the disease when allowed to continue without surgical interference. In a review of 40,621 necropsies from the Eppendorfer Klinik, Kümmell gives 119 cases of tuberculosis of the kidney. In 84 of the cases, the condition was bilateral and in 35, unilateral. In contrast to this, bilateral infection was found in only 5 of 100 surgical cases of renal tuberculosis.

In the cases in which operation was not performed, there was evidence of other foci of tuberculosis in 99.2 per cent and in those in which operation was performed, 44 per cent.

Pugh¹³ reviews the literature and records that in 69 per cent of cases in which exacerbation of unilateral tuberculosis occurred during pregnancy, abortion or nephrectomy became necessary immediately. Thus it would seem that pregnancy, instead of increasing the necessity for conservative treatment of renal tuberculosis, would contraindicate it. As the renal process is acutely exacerbated in 71.1 per cent of the cases.

11. Joly, J. F.: The Late Results of Renal Tuberculosis, *Brit. J. Tuberc.* 19: 188, 1925.

12. Kümmell, H.: Ueber Nierentuberkulose, *Ztschr. f. Urol.* 17:18, 1923.

13. Pugh, W. S.: Tuberculosis of the Kidney in Pregnancy, *Ann. Surg.* 86: 591, 1927.

Nephrectomy is the procedure of choice, although in certain neglected cases preliminary incision and drainage may be indicated. Molesworth advocates preliminary laparotomy, and cites three cases of concurrent peritoneal injury in support of his views; in each of these cases, however, the kidney was removed and the rent in the peritoneum closed through an incision in the loin. In the presence of symptoms strongly suggestive of intraperitoneal injury, exploratory laparotomy is indicated, but if the abdominal contents are found to be uninjured, the wound should be closed and the kidney removed through an incision in the loin.

Analysis of the small series of recorded cases justifies the statement that with the wider application of instrumental diagnostic means, exploration of the abdomen will rarely be indicated in case of rupture of the sac, since, if the true nature of the injury is recognized, one can be reasonably sure that there are no complicating intraperitoneal injuries.

Papin¹⁷ states that in surgical treatment of hydronephrosis, two extremes should be avoided, the essentially conservative and the radical. Conservative treatment was predominant in the earlier period of renal surgical procedures, and was replaced by radical treatment. Differentiation of the cases of hydronephrosis in which surgical treatment should be given and those in which medical treatment should be administered, can be determined only by pyelography. The old surgical procedures consisted of pyeloplicature and other plastic measures on the pelvis and ureter.

Nephropexy serves satisfactorily if the ureter is kinked and is unsatisfactory in cases with small congenital dilatations. The resection of anomalous arteries, which is similar to the so-called resection of Albarran, brings about atrophy of the corresponding renal segment.

Papin resected part of the renal pelvis in 6 cases; this was followed by renal drainage and nephropexy. In 2 cases he performed partial nephrotomy with dilatation and drainage of a large superior calix; in 1 case, partial resection of the kidney was performed and in another case pyelo-ureteral anastomosis.

Ptoxis.—Demel¹⁸ reports his experience in 22 cases of nephroptosis. Operation was performed in 7 of these and there were 3 recurrences. In 1 of the 4 remaining cases a different pain developed, although the renal pain disappeared. The associated pain in 2 other definite cases of removable kidneys disappeared after appendectomy. The remaining 13 patients were not operated on. Seven of these were completely relieved by abdominal binders and 3 were greatly relieved by the wearing of supports.

17. Papin: Les opérations conservatrices dans les hydronephroses, *Presse méd.* 2:1365, 1927.

18. Demel, Rudolf: Ist die Nephroptose ein chirurgisches Leiden? *Beitr. z. klin. Chir.* 139:96, 1927.

It was believed that this was the result of stagnation of blood in dilated vessels and capillaries, thereby leading to bleeding by diapedesis. A series of experiments was also carried out to observe the influence of trauma, and it was concluded that the mechanism of hematoma is due to trauma and to hemorrhagic diapedesis.

Hydronephrosis.—Hellstrom¹⁵ reports two cases of hydronephrosis in which the pelvic dilatation was probably caused by the oblique course through the wall of the pelvis of the upper end of the ureter.

Hellstrom recognizes three types of pathologic change at the ureteropelvic juncture: congenital preformations, inflammatory processes and mechanical change produced through irregular dilatations of the wall of the renal pelvis. In the two first types, therefore, the changes at the ureteropelvic juncture are the primary factors and the cause of hydronephrosis; in the third type the contrary is true. A combination of these three possibilities may occur naturally; it may then be difficult to determine which form is present. In one of Hellstrom's cases, the extrarenal portion of the renal pelvis was about 9 cm. in diameter. The ureter, which was not dilated, arose from the lower wall of the renal pelvis, curved sharply upward and was fixed for about 1 cm. to the anterior wall of the renal pelvis; from there it was unattached and turned downward in an acute angle. In the second case, the kidney was large, dilated and almost completely destroyed. The ureter started from the anterior and medial wall of the renal pelvis about 2 cm. from its lower pole and passed for a distance of about 1 cm. obliquely through the wall of the pelvis from below upward. In a third case, that of a large hydronephrotic sac, the obstruction was believed to have been caused by spastic conditions at the ureteropelvic juncture.

Herman,¹⁶ in reporting a case of rupture of a hydronephrotic sac reviews the literature carefully. The condition is rare, from twenty-five to thirty cases only having been reported.

The case reported was that of a woman, aged 27, who was known to have pyelitis. She had been injured by a motor truck and was admitted to the hospital complaining of pain on the right side. There was tenderness and rigidity over the right flank. Signs of intra-abdominal injury were not present. The urine was bloody. A cystoscopic examination four days after the accident showed bleeding from the right kidney. A week later a pyelogram revealed rupture of a hydronephrotic sac on the right side. Nephrectomy was followed by recovery. (Only two cases are on record in which a correct preoperative diagnosis was made.

15. Hellstrom, John: Contribution to the Knowledge of the Etiology of Hydronephrosis. *Acta chir. Scandinav.* 62:167, 1927.

16. Herman, L.: Case of Ruptured Hydronephrosis. *J. Urol.* 16:452, 1927

roentgen-ray opaque type of catheter is most satisfactory as it resists corrosion for a longer period than the ordinary plain catheter. He uses as large a catheter as possible with a large eye, cutting the meatus if necessary. The results are said to be better with the larger catheters. Pain, if it occurs from the indwelling catheter, is controlled by narcotics.

Corbus and Danforth,²¹ in a study of pyelitis of pregnancy, find that although palliative and conservative measures afforded relief there was evidence of trouble persisting after delivery. In such cases treatment should be instituted after the pregnancy ends, in order, if possible, to restore adequate urinary drainage. In thirteen consecutive cases in which pyelographic studies were carried out after the termination of pregnancy, lesions were demonstrated in the urinary tract. Since lesions were present in the urinary tract after termination of pregnancy in all the cases studied, it seems reasonable to assume that they may have been present before the pregnancy began.

Crabtree²² believes that there is a great deal that is not understood about the relationship of ureteral stricture to pyelitis of pregnancy. He is convinced that if stricture exists in many pregnant women with pyelonephritis, it is of only a few weeks' duration and that the patient recovers spontaneously after delivery. He does not think it is present in the majority of ureteral and pelvic dilatations in pregnancy. The return to normal of such kidneys without treatment for stricture is too rapid, and proper drainage measures will relieve the distention in the absence of ureteral dilatation. Crabtree recognizes that such a statement only adds to the controversy over the "clinical" stricture. In his clinic, he demonstrated in postpartum pyelonephritis an area of inflammatory change in one case sufficient to deform the course of the ureter. Stricture subsequently developed at that point. The severity of inflammatory reaction in the partially closed type of kidney found in the pregnant woman is favorable to the formation of stricture after delivery, on account of the scar tissue. In one case, a stricture developed within a year following pyelographic evidence of its absence.

The evidence available on the subject of the formation of the stricture in pyelonephritis of pregnancy is extremely meager. It is rarely possible to learn the condition of the urinary tract either before or early in pregnancy. Pyelography either during pregnancy or within three months following delivery is unreliable, since interpretations made on pyelograms taken before the kidney has recovered from the distention present during pregnancy are misleading. Different degrees of disten-

21. Corbus, B. C., and Danforth, W. C.: Pyelitis in Pregnancy, *J. Urol.* 18: 543, 1927.

22. Crabtree, E. G.: Stricture Formation in Ureter Following Pyelonephritis of Pregnancy, *J. Urol.* 18:575, 1927.

Demel states that nephropexy should not be performed: (1) in cases in which the anatomic factors are not definitely explained, (2) in cases of generalized enteroptosis, (3) in cases of painless movable kidney; (4) in cases of gastro-intestinal symptoms or (5) if patients are hysterical or neuropathic. Usually nephropexy is not a satisfactory treatment for hydronephrosis associated with movable kidney. The operation should be undertaken only in cases of marked renal pain and distention which is caused by intermittent hydronephrosis or acute obstruction due to circulatory disturbances or kinking of the renal pedicle or of the ureter.

Demel believes that the conservative nonoperative treatment should be attempted usually, and that in most cases it will be successful or partially so.

Pyelonephritis.—Stephen,¹⁹ in discussing pyelitis in children, states that simple bacilluria may exist without cells in the urine. It is difficult to recognize bacilluria without pyuria, and often there is a long course of illness before it is correctly diagnosed. *Bacillus coli-communis* is usually the cause of pyelitis; this term covers several species besides *Bacillus coli-communis* proper, such as lactose fermenters, *Bacillus cloacae* and the *Bacillus lactis-aerogenes* and the nonlactose fermenters, *Bacillus typhosus*, *Bacillus proteus*, Gärtner's bacillus and Morgan's bacillus.

One hundred and eleven of the 148 patients with pyelitis who were treated at the Royal Alexandria Hospital were females. The duration of pyrexia varied from eight to sixteen days. Treatment with alkalis for long periods was usually successful. Alternating the alkalis with methenamine and sodium acid phosphate has been advised, but Stephen obtains the best results by persisting in an uninterrupted course of alkalis.

Infants, 12 months of age, frequently required and tolerate 2 Gm. (30 grains) of sodium bicarbonate and 2 Gm. potassium or sodium citrate three or four times a day. Vaccine has often proved invaluable in the treatment of chronic pyelitis in children, but usually must be continued for several weeks.

If there is a history of definite pyelitis extending over a period of months, the patient should be referred to a urologist for pelvic lavage.

Pugh²⁰ has studied pyelitis of pregnancy and reviews the literature carefully. He believes that urinary antiseptics are of questionable value in this disease and says that treatment should be limited to the use of large draughts of water at frequent intervals. He advises the use of the indwelling catheter as the ideal form of treatment in all cases. The

19. Stephen, E. H. M.: Pyelitis in Children, M. J. Australia 2:142, 1927.

20. Pugh, W. S.: Pyelitis of Pregnancy; Its Treatment with Indwelling Catheter, J. Urol. 18:553, 1927.

He believes that if the patient is ill, drainage should be instituted, and the indwelling ureteral catheter gives the best results. In studying a large series of pyelograms, he has seen dilated calices and pelves which have made him consider the possibility of previous pyelonephritis, but the history did not confirm this; on further investigation, however, he has found this to be the result of previous pregnancies.

Kretschmer does not agree with Eisendrath as to the advisability of routine drainage in cases of acute pyelonephritis by means of the indwelling ureteral catheter. He does not use drainage in those cases except in pregnancy, and then not often.

Hooe states that he left the catheter in one side for eight days and in the other side fourteen days. Untoward results did not follow.

Pyelovenous Back-Flow.—Gile²⁴ reports a comprehensive group of experiments which he recently carried out in the hope of determining the mechanism of pyelovenous back-flow. In corrosion specimens of the renal pelvis of cadaveric specimens, venous outbranchings were not obtained except when extravasation had occurred.

The results from injections of dye were similar to those of Hinman; the venous system was injected regularly, the tubules were never more than partially injected and this rarely. Roentgen-ray observations of opaque solutions injected confirmed those made by Hinman. None of these observations, however, demonstrate how the substances reach the blood stream from the pelvis. Normally, there is no intrapelvic pressure. Under a positive pressure, there may be microscopic ruptures, filtration, osmosis, increased permeability of the pelvic membrane, lymphatic absorption or the opening up of a direct communication already present in the angles of the minor calices as suggested by Hinman.

The tubules are undoubtedly partially injected, but since dye is found in the blood vessels and not in the tubules following injection of living mammalian kidneys, it would seem that they are not significant in the production of back-flow.

The living kidney of the frog apparently presents a different mechanism, as in it the tubules were easily filled.

The term "pyelovenous back-flow" is illustrative, if it is understood in a general sense, of the passage of substances from the renal pelvis to the venous circulation. Probably this phenomenon does not occur by way of the tubules; its exact route has not yet been demonstrated.

24. Gile, H. H.: Observations on Injections of the Renal Pelvis, *J. Urol.* 18:621, 1927.

tion of such pelvises will give entirely different pictures. The slack following distention has not yet been considered.

Pugh has found that the stricture occurs in the ureter at points where there can be no pressure from the fetus; it is the result of inflammatory changes attendant on pyelonephritis of pregnancy. It is noteworthy that the few strictures which have been observed in the pregnant women of his clinic did not cause symptoms immediately after delivery but months afterward.

Eisendrath²⁸ makes a plea for the more widespread use of the inlying ureteral catheter in the treatment of persons with pyelonephritis and other renal conditions. Ordinarily, in lavage of the renal pelvis, the ureteral catheter is withdrawn immediately.

The inlying catheter, first recommended for the relief of obstructive aneuria and nontuberculous renal infections, now is used: (1) for the relief of aneuria of the obstructive type, (2) in the treatment of patients with acute and chronic pyelonephritis, (3) for relief from pain resulting from ureteral obstruction, (4) in cases of ureteral injury following pelvic operations, and (5) as a method of drainage of the kidney after the repair of a vesicovaginal fistula.

Eisendrath employs small roentgen-ray ureteral catheters, as the coating is more durable on the opaque than it is on the nonopaque catheter. Only a single catheter is inserted into the ureter of the affected side. Irrigation of the renal pelvis is not necessary, as there is ample drainage through the lumen or alongside the inlying catheter. The time the catheters can be left in place varies. If they tend to be expelled, a small urethral catheter can be introduced into the bladder to avoid accumulation of urine.

Crosbie, in discussing Eisendrath's paper, states that he believes drainage should be reserved for cases of obstruction, in which the pelvis of the kidney cannot drain itself. A ureteral catheter cannot be left in long without causing a certain amount of injury to the ureter.

Merritt states that he had found the failure to irrigate the renal pelvis to be the cause of catheter blockage in many cases, and for this reason he now uses two catheters irrigating with sterile water and then a solution of mercurochrome-220 soluble through one.

Livermore maintains that stasis is the chief cause of infections of the kidney. Although there may be a definite focus of infection, it does not lodge in the kidney unless stasis is present or the dosage overwhelming. If there is obstruction, the kidney will unquestionably be infected.

Bumpus states that another type of case which has not been mentioned in the treatment with the inlying catheter is pyelitis of pregnancy.

23. Eisendrath, D. N.: Inlying Ureteral Catheter in Treatment of Pyelonephritis and Other Renal Conditions, *J. A. M. A.* 89:2170 (Dec. 24, 1927).

duced experimentally in the living dog by the administration of ether. A further possible source of this fat is suggested by the present study.

The presence of fat embolism following death from causes other than trauma has been remarked by several observers. Scriba² found fat embolism present in 52 per cent of all bodies. In addition, many specific diseases have been found to be associated with fat embolism. To put these on record in juxtaposition to our present results, we quote the following paragraph from our previous report:¹

Carrara³ reports fat embolism present at necropsy in 22 per cent of deaths from cardiovascular-renal disease and in 44 per cent of burns. Catsaras⁴ found fat emboli in the lungs in eighteen of sixty-seven cases of postinfluenzal pneumonia. Gröndahl⁵ reports fat embolism in two cases of eclampsia, four cases of diabetes, and two cases of phosphorus poisoning; Winkler⁶ in two cases of acidosis, and Winogradow⁷ as occurring regularly in potassium chlorate poisoning. In addition to these repeated findings there have been authentic reports of fat embolism having occurred, without history of trauma, in one or more cases of each of the following conditions: carbon monoxide poisoning,⁸ profound sepsis,⁹ chronic alcoholism,⁸ chloroform narcosis,⁸ diabetic retinitis,⁸ phlegmonous gastritis,⁸ acute pancreatitis,⁸ chronic tuberculosis,⁸ menstrual suppression, hepatitis, splenitis, carcinomatosis and sarcomatosis.⁸ (The last five conditions are cited from the literature by Warthin.)

On account of the generally accepted observation that if fat embolism occurs, it will be seen in the lung (because of the slower blood current and unsupported capillary walls), our observations were limited to lung tissue. This limitation gave us also a simpler standard for comparison. We have examined the available lung tissue in fifty unselected cases that were subjected to autopsy by the department of pathology of Washington University. These cases were not numerically consecutive, but they were consecutive with the necessary proviso that lung tissue had been preserved and filed. They were known to us by serial number until the tissue had been sectioned, stained and diagnosed for fat embolism. Sudan III was uniformly used for staining. After our diagnoses were recorded, we referred to the files of the pathologic department for postmortem diagnoses. We thereby prevented any preconceived ideas from influencing the result.

It is to be noted that the material available consisted of only one piece of tissue in most cases. In those instances in which disease of the lung was present, the specimen usually included the diseased portion of the

2. Scriba: *Deutsche Ztschr. f. Chir.* 12:118, 1879.

3. Carrara: *Freidreich's Bl. f. gerichtl. Med.*, 1898, vol. 49.

4. Catsaras, J.: *Presse méd.* 26:618 (Sept. 4) 1920.

5. Gröndahl: *Deutsche Ztschr. f. Chir.* 111:56, 1911.

6. Winkler: *Ztschr. f. orthop. Chir.* 45:616, 1924.

7. Winogradow: *Virchows Arch. f. path. Anat.* 190:92, 1907.

8. Bantin, C. F.: *Diabetic Lipemia Retinalis and Fat Embolism*, J. A. M. A. 86:546 (Feb. 20) 1926.

9. Warthin: *Internat. Clin.* 4:171, 1913.

FAT EMBOLISM

II. INCIDENCE AT POSTMORTEM *

EDWIN P. LEHMAN, M.D.

UNIVERSITY, VA.

AND

ROBERT F. McNATTIN, M.D.

ST. LOUIS

In an earlier report on uncompleted studies on fat embolism,¹ the conclusion was reached that fat embolism is not necessarily traumatic in origin. This conclusion was based partly on experimental work and partly on published reports of the occurrence of fat embolism in non-traumatic cases. At that time, our personal experience did not include any instances of the latter type in the human being. Further, we found that search for fat emboli is not a routine in pathologic examination post-mortem. It therefore seemed desirable to check earlier authors by a search through unselected postmortem material for cases of fat embolism.

In our previous observations, the question was also raised as to the problematic rôle of fat embolism in the production of symptoms and death even in extremely severe cases. We found that dogs would tolerate without symptoms an amount of free fat in the blood stream considerably greater, weight for weight, than the amount that could be freed in the human being by the ordinary fracture, even of the femur. Our conclusions on this figure are somewhat modified by later injection experiments now being prepared for publication; nevertheless, we shall report a discrepancy in tolerance that still casts doubt on certain post-mortem diagnoses of fat embolism as a cause of death. It was hoped that the present series of examinations of material observed at autopsy would yield information concerning the quantity, distribution and character of fat emboli in various disease states that might throw some light on this second question.

In our earlier studies, we concluded that the fat found as embolism in nontraumatic cases probably appeared by the coalescence of the ultra-microscopic particles of fat normally occurring in the blood plasma. This coalescence was attributed to a breaking down of the physiologic emulsion from physical or chemical changes in the blood and was pro-

*From the Department of Surgery of Washington University and the Barnes Hospital.

1. Lehman, E. P., and Moore, R. M.: Fat Embolism: Including Experimental Production Without Trauma. *Arch. Surg.* 14:21 (March) 1927

TABLE 1.—*Degree of Embolism in Fifty Unselected Cases*

| NO FAT EMBOLISM | | Age | Operation | Trauma |
|------------------------------------|--|-----------|---------------------------|----------------|
| No Fat | | | | |
| 2901 | Prematurity | Premature | 0 | 0 |
| 2909 | Acute purulent mastoiditis; hemorrhage into brain | 10 wks. | 0 | 0 |
| 2913 | Asthma, bronchial; bronchitis, acute and chronic | 60 | 0 | 0 |
| 2945 | Congenital atresia, common hepatic duct..... | 6 wks. | 0 | 0 |
| 2952 | Enterocolitis, acute; bronchopneumonia..... | 4½ mos. | 0 | 0 |
| 2968 | Tumor of cerebellum..... | 29 | 7 mos. ago 24 hrs. ago | 0 |
| 2984 | Congenital heart disease..... | 6 mos. | 0 | 0 |
| 2986 | Coronary thrombosis; rupture of heart..... | 50 | 0 | 0 |
| 3006 | General purulent peritonitis following perforation of gastric ulcer..... | 49 | 5 days ago | 0 |
| 3008 | Carcinoma of head of pancreas, metastasis to liver | 55 | 0 | 0 |
| 3315 | Miliary tuberculosis (general) 3 weeks, post-partum | 25 | 0 | 3 wks. (labor) |
| Leukocytic Fat Only | | | | |
| 2949 | Acute bacterial endocarditis, four transfusions | 28 | 0 | 0 |
| Fat in Alveolar Exudate Only | | | | |
| 2947 | Pulmonary tuberculosis; tuberculous pneumonia | 24 | 0 | 0 |
| FAT EMBOLISM | | | | |
| Slight | | | | |
| 2905 | Lobar pneumonia; chronic tuberculosis..... | 52 | 0 | 0 |
| 2910 | Acute lymphatic leukemia..... | 2 | 0 | 0 |
| 2916 | Excision of cecum; acute suppurative peritonitis | 6 | Recent | 0 |
| 2922 | Endocarditis, chronic and acute; pulmonary thrombosis | 44 | 0 | 0 |
| 2925 | Glioma of brain..... | 30 | Recent | 0 |
| 2931 | Glioma of brain; hemorrhage, postoperative... .. | 5 | Recent | 0 |
| 2936 | Cholecystitis and cholelithiasis; general peritonitis; abscesses of liver..... | 50 | 6 days ago | 0 |
| 2938 | Acute purulent otitis media and mastoiditis, bilateral | 2 mos. | 0 | 0 |
| 2941 | Endocarditis, chronic | 39 | 0 | 0 |
| 2946 | Acute lobar pneumonia..... | 45 | 0 | 0 |
| 2950 | Carcinoma of stomach, with metastases..... | 43 | 0 | 0 |
| 2951 | Hypertrophy and dilatation of heart; endocarditis, chronic | 40 | 0 | 0 |
| 2955 | Abscess of lung; pyemia..... | ? | 0 | 0 |
| 2958 | Adenoma of thyroid; auricular thrombus..... | 59 | 0 | 0 |
| 2962 | Polycystic kidney, bilateral..... | 42 | Recent | 0 |
| 2964 | Cellulitis of thigh, with abscess; bronchopneumonia | 46 | 2 days ago | 0 |
| 2965 | Aneurysm of arch of aorta (wiring operation) | 51 | 1 year ago | 0 |
| 2989 | Lobar pneumonia; empyema, thoracic..... | 33 | 0 | 0 |
| 2994 | Status lymphaticus; old operative scar for nephrostomy | 1½ | Old | 0 |
| 3010 | Chronic myelogenous leukemia; bronchopneumonia | 26 | 0 | 0 |
| 3011 | Toxemia of pregnancy; incision, peritonsillar abscess | 36 | Recent | 0 |
| 3020 | Syphilis, congenital | 4 mos. | 0 | 0 |
| Moderate | | | | |
| 2883 | Carcinoma of cervix; acute pelvic peritonitis... .. | 42 | 0 | 0 |
| 2895 | Carcinoma of kidney; pyonephrosis..... | 52 | 0 | 0 |
| 2914 | Toxemia of pregnancy; retained placenta..... | 21 | 0 | Recent (labor) |
| 2930 | Abscess, subdiaphragmatic; cholecystectomy.... | 50 | Recent | 0 |
| 2957 | Mastoiditis, acute, bilateral; paracentesis tympani | 15 days | Recent (see col. 2) | 0 |
| 2961 | Fracture, ribs, multiple; emphysema, subcutaneous | 86 | 0 | Recent |
| 2975 | Arterial sclerosis, involving coronary artery.... | 58 | 0 | 0 |
| 2996 | Hypertrophy of prostate; pyelonephritis; pericarditis, adhesive | 49 | 0 | 0 |
| 3005 | Chronic ulcerative colitis with polyposis; acute purulent peritonitis; ileostomy..... | 54 | Recent | 0 |
| 3017 | Aneurysm of abdominal aorta with rupture; syphilis | 62 | 0 | 0 |
| Marked | | | | |
| 2933 | Subperiosteal abscess, femur; suppurative arthritis, hip; pyemia..... | 7 | 0 | 0 |
| 2935 | Adenocarcinoma, colon, with metastases; spontaneous fistula | 57 | 8 days ago | 0 |
| 2930 | Arthritis, knee, suppurative; thrombosis of coronary artery; incision and drainage, knee joint | 63 | Day of death | 0 |
| Embolism in Single Area of Section | | | | |
| 2906 | Lymphatic leukemia | 52 | 0 | 0 |
| 2923 | Glioma of pons; bronchopneumonia..... | 35 | Recent | 0 |

organ. It is possible that this fact influenced the results; however, as intracapillary fat was sought, the presence of disease, such as pneumonia or tuberculosis, should tend rather to diminish the fat found through inflammatory occlusion of capillaries. If fat was found in the vessels of a small segment of one lung in nondiseased areas, the conclusion that it occurred elsewhere in the lungs is highly probable.

Intracapillary globules of fat, except as discussed later in relation to fat found in the phagocytes, were diagnosed as fat embolism. Most of these were large enough actually to plug capillaries. The number of these was estimated, and the degree of embolism classified as shown in table 1. "Slight" fat embolism (table 1) was diagnosed when considerable search through a section was necessary before fat was found. "Moderate" fat embolism (table 1) signifies that the fat was easily found, but not in the majority of microscopic fields. "Marked" fat embolism (table 1) means that fat was found in the majority of fields. In two cases, the embolism found was limited to one area of the section. These two cases were given a separate classification (table 1) on the chance that this distribution might invalidate the diagnosis. For the reasons to follow, however, it is permissible to assume other areas elsewhere in one or both lungs.

As we have observed in our experiments on injection of fat ¹⁰ and in these present specimens, even marked grades of embolism are patchy in distribution. This is shown by areas of intense distribution of fat next to areas free from fat. For this reason, the demonstration of a few definite fat emboli (as listed in table 1) must be considered positive instances of fat embolism.

We did not find fat tissue in the peribronchial zone in the human material studied as we did in the dog. This may be because a block of tissue in the former does not reach the major bronchial ramifications as a block of the same size does in the latter.

Phagocytes containing fat were rather less regularly observed in the human being than in the dog. This probably can be ascribed to the fact that death in the human being is frequently preceded by starvation as it is not in the experimental animal. We were careful, however, to assure ourselves that no fat diagnosed as emboli was in the bodies of phagocytes. Occasionally, we found collections of fat-containing leukocytes and in the same zone much intracapillary fat (fig. 1). In one instance, this was entirely in the form of minute droplets of the same size as those in the cells. This was reported as showing only leukocytic fat (table 1). In other instances, in addition to such small droplets, globules larger by several diameters than any found in the cells were present. These droplets were reported as emboli. It seems possible that a source of free fat in the blood stream may be the destruction of fat-containing leukocytes as well as the breaking down of the physiologic emboli of

10. Lehman, E. P., and McNattin, R. F.: To be published.

The results of this study confirm earlier conclusions that fat embolism is an extremely common postmortem observation in all kinds of conditions, traumatic and nontraumatic. If the proportion found in this series of fifty cases should hold true through a larger experience, more than

TABLE 2.—*Proportionate Division of Fat Embolism in Fifty Unselected Lungs*

| | | | Per Cent |
|------------------|----|-----|----------|
| No embolism..... | | 13 | 26 |
| Embolism..... | | 37 | 74 |
| Slight..... | 22 | 44% | |
| Moderate..... | 10 | 20% | |
| Marked..... | 3 | 6% | |
| Single area..... | 2 | 4% | |
| Total..... | | 50 | |

TABLE 3.—*Relationship of Trauma to Occurrence of Fat Embolism in Fifty Unselected Lungs*

| | No Fat Embolism | Per Cent |
|-------------------|-----------------|----------|
| Traumatic..... | 3 | 23 |
| Nontraumatic..... | 10 | 77 |
| | 13 | |
| | Fat Embolism | |
| Slight | | |
| Traumatic..... | 9 | 41 |
| Nontraumatic..... | 13 | 59 |
| Moderate | | |
| Traumatic..... | 5 | 50 |
| Nontraumatic..... | 5 | 50 |
| Marked | | |
| Traumatic..... | 2 | 66.6 |
| Nontraumatic..... | 1 | 33.3 |
| Single areas | | |
| Traumatic..... | 1 | 50 |
| Nontraumatic..... | 1 | 50 |
| | Summary | |
| Traumatic..... | 17 | 46 |
| Nontraumatic..... | 20 | 54 |
| | 37 | |

TABLE 4.—*Occurrence of Fat Embolism in Traumatic and Nontraumatic Cases in Fifty Unselected Lungs*

| | | Per Cent |
|-------------------------|----|----------|
| Traumatic cases..... | 20 | |
| No embolism..... | 3 | 15 |
| Embolism..... | 17 | 85 |
| Nontraumatic cases..... | 30 | |
| No embolism..... | 10 | 33.3 |
| Embolism..... | 20 | 66.6 |

half of all fat embolism is not associated with trauma. The variety of diagnoses in nontraumatic cases in which we have found fat embolism is great. Certainly no one influence can be detected. Although, in our tables, the assumption is made that trauma is the determining cause of fat embolism in those cases in which it occurs in the history, the frequent

the plasma in nontraumatic cases. This is borne out by the fact that, with the one exception noted, whenever leukocytes were filled with fat, embolism also occurred.

The statistical analysis of the results of this study is reported in tables 2, 3 and 4. Of course, in such a small series, no emphasis can be put on the actual percentage estimations as indicating definite rates of incidence. They serve, however, to make certain conclusions tenable. The striking facts obtained from this analysis are as follows: 1. Definite fat embolism occurs in more than half of all lungs examined at

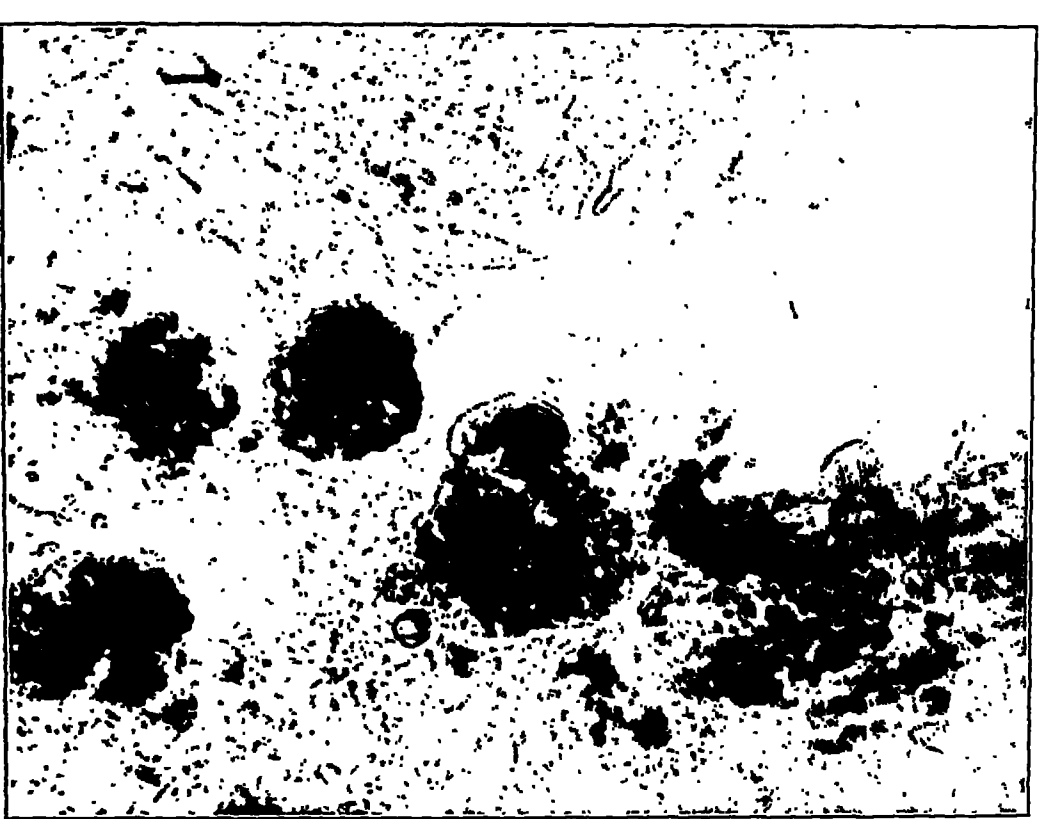


Fig. 1.—Fat emboli and fat-filled phagocytes; showing the difference in size between globules of free fat diagnosed as emboli and the much more minute particles in the cells (autopsy no. 2935); $\times 986$.

autopsy (table 2). 2. About one half of the lungs in which fat embolism occurs are from patients in whom there has been no history of trauma (table 3). 3. In a small proportion of cases in which definite trauma is recorded, no emboli could be found in a single examination of one lung (table 3). 4. Fat embolism is found in an overwhelming proportion of lungs from patients subjected to injury or operation (table 4). 5. Fat embolism occurs in more than half of the miscellaneous fatal diseases without history of trauma (table 4).



Fig. 4.—Fat emboli in a case of toxemia of pregnancy with retained placenta (autopsy no. 2914); $\times 986$.

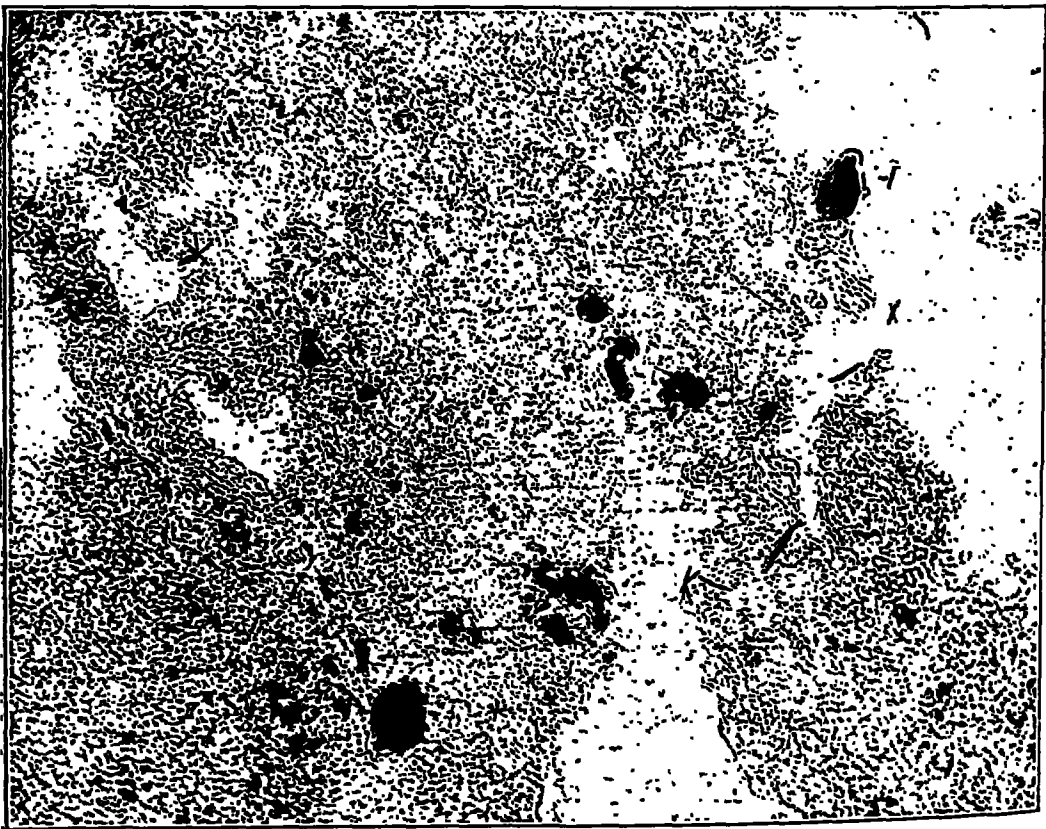


Fig. 5.—Fat emboli in case of suppurative arthritis of hip with subperiosteal abscess of femur in which operation was not performed (autopsy no. 2933). Low power magnification was used to show large number of emboli.



Fig. 2.—From a case of tuberculous pneumonia; showing free fat and fat-filled cells in the alveolar exudate and no fat in the alveolar walls (autopsy no. 2947). This illustrates a possible fallacy in Warthin's sign; $\times 490$.

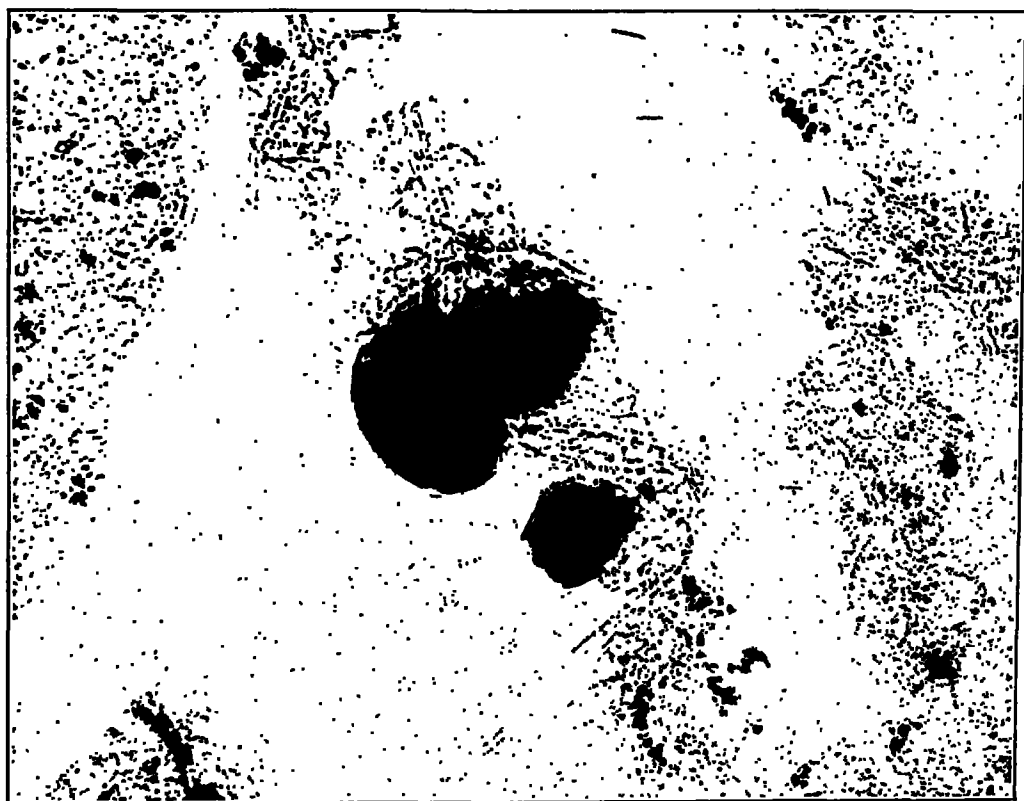


Fig. 3.—Fat emboli following multiple fractures of the rib (autopsy no. 2961). Here a globule of fat appears to be partially extruded into the adjacent alveolus, illustrating the mechanism of the appearance of fat in the sputum (Warthin's sign of fat embolism); $\times 490$.

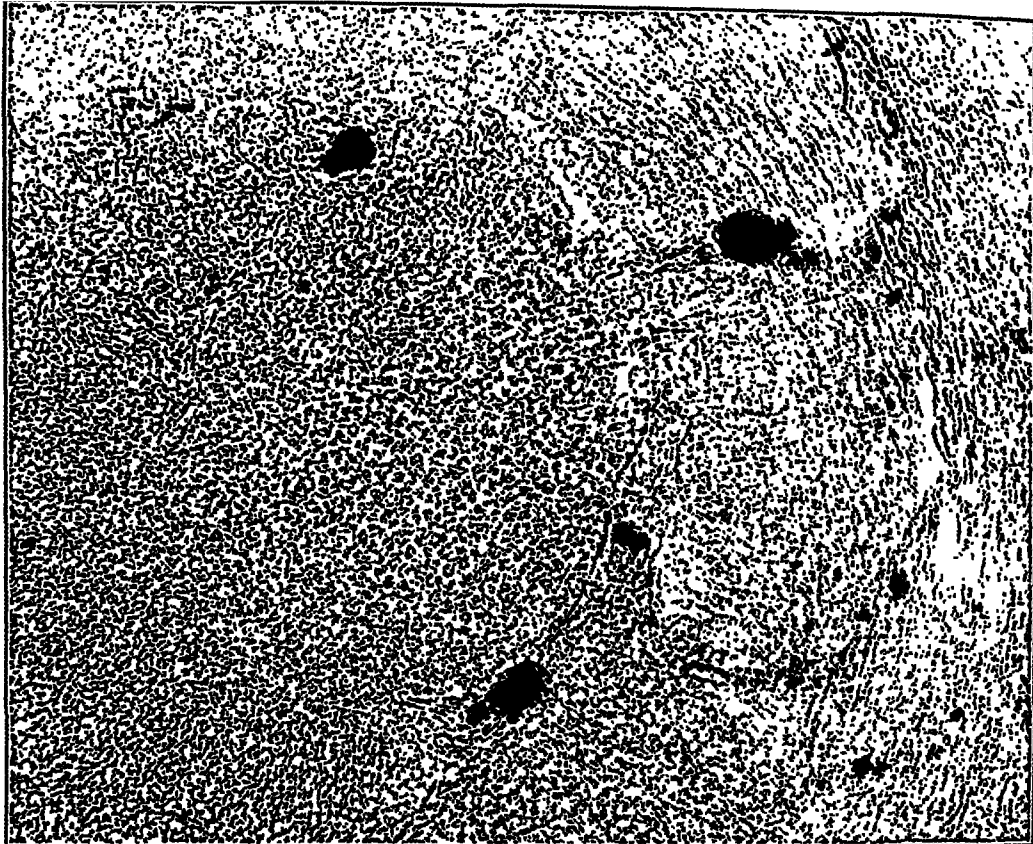


Fig. 7.—Slight degree of fat embolism (autopsy no. 2905). Postmortem diagnosis was lobar pneumonia and chronic tuberculosis. Three emboli were found in a single field; $\times 183$.

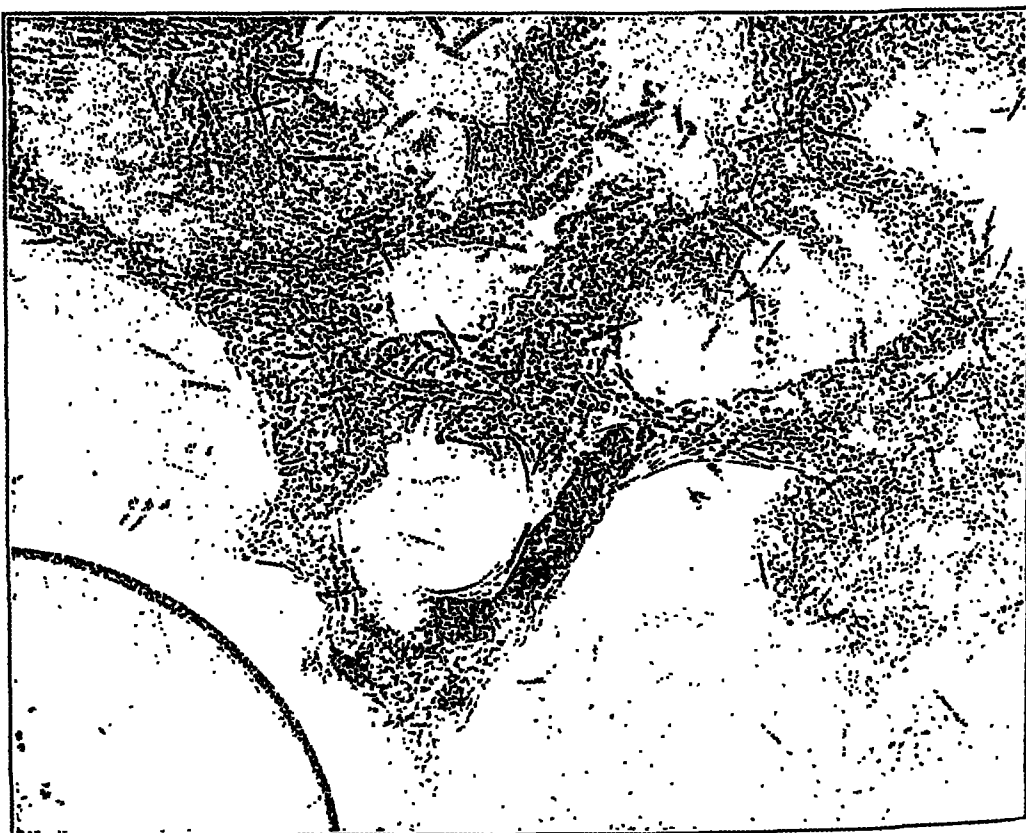


Fig. 8.—Several fat emboli in a case of carcinoma of the kidney and pyonephrosis (autopsy no. 2895); $\times 198$. Precipitated crystals of Sudan III are seen in this and other photomicrographs.

occurrence of fat embolism in nontraumatic fatal disease makes such an assumption not necessarily true. In other words, in some of the cases reported as due to trauma, other factors may conceivably have been the true cause.

What these factors are is a pressing problem. As reported earlier, there is certain experimental evidence that they may consist in physical and chemical changes in the blood, converting the physiologic emulsion of the plasma into free fat. This has been accomplished in the dog by the administration of ether. In studies of artificial emulsions in the test tube,



Fig. 6.—Fat emboli in case of suppurative arthritis of knee with coronary thrombosis. This patient was subjected to incision and drainage of the knee joint on the day of death (autopsy no. 2960); $\times 490$.

there is suggestive evidence that the products of protein decomposition may possibly be blamed. Further studies along these lines have so far not been successful in confirming this suggestion.

When one considers these facts together with the experiments already referred to, one is forced to the conclusion that the presence of fat embolism in the lung after trauma does not justify the conclusion that such fat has been caused by the trauma or that it has caused death. Unquestionably there are cases of multiple fractures showing immediate symptoms, early death and blood at postmortem loaded with fat,

ARTERIOVENOUS ANEURYSM OF THE BRAIN*

WALTER E. DANDY, M.D.
BALTIMORE

The intracranial arteriovenous aneurysms here described are not peculiar to the brain. With the exception of differences of detail due to environment, they are essentially the same as arteriovenous aneurysms situated elsewhere in the vascular system.

The discovery of an arteriovenous aneurysm is always credited to William Hunter.¹ Enthusiastic phlebotomists of that period prepared two perfect examples of arteriovenous aneurysm for Hunter, which he was quick to recognize. His description of the signs and symptoms left little to be added, even at the present time. At the point of the communication between the artery and the vein, he recognized a loud hissing murmur and a strong tremulous thrill; large tortuous venous sacs were seen to pulsate; the brachial artery was greatly enlarged and serpentine cephalad to the arteriovenous fistula, but distal to it, the artery became smaller than on the other side. He was able to reduce the size of the veins, stop their pulsation and eliminate both the murmur and the thrill by pressing on a localized spot, which he recognized to be the opening between the artery and the vein. It was Hunter who first suggested the term "anastomosis" to denote the union of the two vessels.

To arteriovenous aneurysms of traumatic origin have since been added a great group with precisely the same clinical features, but in which the characteristic vascular changes have been present since birth. Virchow² referred to cases of Krause (Wm.) and Breschet as demonstrating beyond doubt the congenital origin of such cases. He also mentioned a case which Langier watched during the patient's life and in which he performed dissection after the patient's death; a free communication was found between the posterior auricular artery and a nearby vein. There are now many cases in which dissections of these aneurysms at operation or necropsy have demonstrated communication between a large artery and a contiguous vein by one or more aberrant vessels which could have arisen only as errors of vascular development in the embryo. In recent years, remarkable examples of these anomalous congenital communications in the neck and extremities, as disclosed at operation, have been reported by Halsted,³ Rienhoff⁴ and Reid.⁵

* From The Johns Hopkins Hospital and University.

1. Hunter, W., cited by Callender: *Bull. Johns Hopkins Rep.* 19:260, 1920.

2. Virchow: *Die Krankhaften Geschwülste*, Berlin, 1863, vol. 3.

3. Halsted, W. S.: *Congenital Arteriovenous and Lymphaticovenous Fistulae*, Tr. Am. Surg. Ass., 1919.

4. Rienhoff, Jr., W. F.: *Congenital Arteriovenous Fistula*, *Bull. Johns Hopkins Hosp.* 35:271, 1924.

5. Reid, M. R.: *The Effect of Arteriovenous Fistula upon the Heart and Bloodvessels*, *Bull. Johns Hopkins Hosp.* 31:43, 1920.

in which so far as we know at present, it must be considered that the patients died of fat embolism. On the other hand, in any case of trauma with delayed symptoms, no matter how rich the blood in free fat, one must question the direct relationship of the trauma to the fat embolism and the relationship of the fat embolism to the symptoms. It is at least conceivable that the influences causing symptoms and death are also the influences causing freeing of fat in the blood stream.

There is one interesting note to be added. In a case of tuberculous pneumonia observed at autopsy (table 1, no. 2947), a large amount of fat was found in the alveolar exudate and none in the blood vessels (fig. 2). It is, of course, common to observe fat in the alveoli when fat embolism is present (fig. 3). On this basis, Warthin's sign of fat embolism was devised, namely the presence of fat in the sputum. The present observation demonstrates that fat can occur in the air spaces of the lung without embolism; in other words, Warthin's sign may not be as clearcut as is generally thought.

and eliminating not only capillaries but even the great venous and arterial trunks of the early embryo. It is evident that the retention of the original vascular connections between arteries and veins will readily explain the origin of the adult arteriovenous aneurysms. Dr. Halsted had in mind the arteriovenous aneurysm with aberrant congenital connecting channels. But it would seem that the maldevelopment of the original vascular bed would similarly explain the nests of abnormal vessels which are interposed between the arteries and veins and which replace the normal capillary bed.

Arteriovenous fistulas of traumatic origin are practically impossible in the brain, because the principal arteries and veins are not in juxtaposition as are the vessels of the head, neck and extremities. Arteriovenous aneurysms between the internal carotid artery and the cavernous sinus are exceedingly common, but as they are really outside the cranial chambers, and as they are in point of origin rather laws unto themselves, they need not be considered here. They are dependent on an anatomic arrangement which is not duplicated anywhere in the body. As the internal carotid arteries traverse the cavernous sinus in their passage through the base of the skull, a traumatic rupture of one of the arteries by a fracture of the base of the skull must inevitably result in an arteriovenous fistula, unless or until the arterial opening is repaired. The nomenclature of lesions which should really be included under arteriovenous aneurysms is most confusing. Being so dependent on the personal equation for the interpretation, they are reported under many titles, i.e., *angioma cavernosum*, *varix aneurysmaticus*, *angioma arteriale racemosum*, *angioma plexiforme*, *aneurysma cirsoidea*, *aneurysma serpentina*, *aneurysma anastomotica*, arteriovenous aneurysm, tumor cirsoideus, and particularly by the Germans as *Rankenangiom*—a term first applied by Virchow. Rienhoff⁴ suggested a simple and sensible revision of the nomenclature of all vascular dilatation and communications into (1) venous, (2) arterial and (3) arteriovenous aneurysms, thereby discarding the term hemangioma at least for major lesions. This classification meets my full approval. In the group of arteriovenous aneurysms, the various terms "cavernous," "racemose," "cirroid" and "serpentine," whether applied to arteries or veins, are merely descriptive of a superficial expression of a lesion and not of the fundamental pathologic process. A long as the term hemangioma is employed when an arteriovenous connection exists, there must always be uncertainty as to whether the tumor is arterial or venous. As a matter of fact, they may be either or both, but regardless of these superficial differences there is a direct communication through the vascular abnormality which has replaced the normal capillary bed. Moreover, the outward expression of an arteriovenous aneurysm, i.e., the arterial tortuosity and dilatation and the

Finally, there is a third group of cases in which an arteriovenous communication is established through the medium of a mass of abnormal vessels which take the place of the usual capillary bed, erroneously known as angiomas because of the impression that they are new growths; the true character of these lesions has long been obscured. The component vessels may be atypically arterial or venous, or both may be combined. Virchow discussed these tumors at length, and with some hesitation classified them under the heading "angioma racemosum arteriale." The following excerpt from his "Krankhaften Geschwülste" shows his grasp of the real underlying pathologic process:

Finally there remains that form of angioma, in which the vascular enlargement is outspoken and in which the character of the tumor is more in the background. Many of these forms are not to be understood in the light of oncology. They are often classified with angiomata and one cannot make a true line of demarcation between them and angiomata. Their difference lies principally in the fact that the process is diffuse, and that dilatation of both arteries and veins is present. These tumors have recently been called by John Bell aneurysma per anastomosin, and by Walker perhaps better, aneurysma anastomoseon.

Another group of vascular tumors so well known, even at the present time, as angioma cavernosum, were included by Bell under his aneurysms per anastomosin. Virchow referred to Dupuytren's experiments to prove that in these tumors injections of colored substance passed freely from the artery into the veins through the intermediary tumor. Virchow, though not conceding the arteriovenous communication, noted the fact that in some cases of cavernous angiomas (venous tumors) the artery is dilated and tortuous just as in true arteriovenous aneurysms.

It was Virchow's view that these arteriovenous aneurysms (or angiomas) were not new growths in the usual sense, but were of congenital derivation. Subsequent embryologic and pathologic researches demonstrated that no other explanation is tenable.

Professor Halsted,³ whose interest in this subject extended over a period of several years, and who stimulated the splendid researches and publications of Callender,⁶ Reid,⁵ Holman⁷ and Rienhoff,⁴ approached the origin of arteriovenous aneurysms from the vascular anlage in the early embryo. It is known that the adult system of arteries and veins is derived from a general capillary network; that both arteries and veins form from this capillary network; that the final arterial and venous systems are derived by extensive evolution of a vastly different primitive system. This metamorphosis is accomplished by shifting, consolidating

6. Callender, C. L.: Study of Arteriovenous Fistula with an Analysis of Four Hundred and Forty-Seven Cases, Johns Hopkins Hosp. Rep. 19:260, 1920.

7. Holman, E. F.: Physiology of an Arteriovenous Fistula, Arch. Surg. 7:64 (July) 1923.

been included, though the status of both is doubtful because the description of the venous outlets is inadequate. Several cases heretofore classified as cases of angioma, and usually assumed to be similar to those collected here, have been excluded. Among them are the cases of Oppenheim,¹⁷ Sweasey-Powers,¹⁸ Lewandowsky and Selberg,¹⁹ Cassirer and Mühsam,²⁰ Uyematsu,²¹ Creite, Abrikosoff,²² Lechner,²³ Versé,²⁴ Rossolimo²⁵ and Bruns. It has also not been possible to include the cases of Isenschmid,²⁶ because neither observations made at operation nor those made at autopsy establish the clinical diagnosis. In one of his cases at least, the diagnosis is almost surely correct for, in addition to a well defined extracranial arteriovenous aneurysm, Jacksonian epileptic attacks were of long standing. The symptoms that I have considered essential for the diagnosis of an arteriovenous aneurysm have been, first and foremost, marked fulness and enlargement of the veins of exit; second, an increased size and tortuosity of the artery entering the snarled mass of vessels. Without the enlarged veins on the cortex or elsewhere one cannot assume the existence of an arteriovenous fistula.

The seeming infrequency of this lesion cannot be judged by the small number of cases assembled from the literature. Were this true, the lesion would be rare indeed. The eight cases which occurred at the Johns Hopkins Hospital among about 600 cases of verified tumors of the brain during a period of five years, are perhaps a better index of its relative frequency. In clinics on which neurologic material is concentrated, arteriovenous aneurysms apparently occur in from about 0.5 to 1 per

17. Oppenheim, H.: Die Geschwülste und die syphilitischen Erkrankungen des Gehirns, in Nothnagel's Practice, vol. 9, p. 20.

18. Sweasey-Powers, W. J.: Ein Fall von Angioma cavernosum des Gehirns, *Ztschr. f. ges. Neurol. u. Psychiat.* **16**:487, 1913.

19. Lewandowsky, M., and Selberg, F.: Ueber Jacksonsche Krämpfe mit tonischem Beginn und über ein kleines Angiocavernom des Gehirns, *Ztschr. f. d. ges. Neurol. & Psychiat.* **19**:336, 1913.

20. Cassirer and Mühsam: *Berl. klin. Wchnschr.* **17**:755, 1911.

21. Uyematsu, S.: A Case of Haemangioma Cavernosum of the Cerebrum, *J. Nerv. & Ment. Dis.* **52**:388, 1920.

22. Abrikosoff, A. S.: Ein Fall von Angiona arteriale racemosum der Arterial basilons und der beiden arterial communicans posterior, *Zentralbl. f. allg. Pathol.* **22**:210, 1911.

23. Lechner, Ellen: Ein Beitrag zur Kasuistik der Hirnangiome, *Beitr. z. klin. Chir.* **125**:174, 1922.

24. Versé: Demonstration eines in die Substanz des Kleinhirns eingebetteten Aneurysma serpentinum et sacciforme der Arteriae Cerebri posterior Sinistra, *München. med. Wchnschr.* **58**:544, 1911.

25. Rossolimo, G. S.: Zum Ausgang von Gehirnoperationen, *Deutsche Ztschr. f. Nervenhe.*, vol. 6; *Neurol. Zentralbl.* **15**:714, 1896.

26. Isenschmid, R.: Die klinische Symptome des cerebralen Rankenangioms, *München. med. Wchnschr.* **59**:243, 1912.

engorgement of the veins leaving the tumor, are doubtless identical whether the communicating channels are exclusively arterial or venous or predominantly one or the other.

In attempting to gather the cases of arteriovenous aneurysms of the brain, the records of venous aneurysms and the various subdivisions of angiomas have been reviewed, and most of them have been collected from these groups. For example, there is no more perfect example of an arteriovenous aneurysm than the one pictured in Krause's colored plate,⁸ but which he calls a venous angioma. On the other hand, cases reported as Rankenangioma and cirroid aneurysma, and therefore presumably arteriovenous aneurysms, have been excluded from this group because the absence of changes in the arteries and veins leading to and from the tumor has suggested a pure venous lesion. Other cases reported as venous, which undoubtedly seem to be arteriovenous, are those of Astwazaturoff,⁹ Steinheil,¹⁰ Dürck, Kalischer,¹¹ Mühsam,¹² Eiselberg,¹³ Campbell and Ballance¹⁴ and others. Doubtless the teaching of Oppenheim and Krause was in large part responsible for the interpretation of these vascular lesions as venous.

FREQUENCY OF ARTERIOVENOUS ANEURYSMS OF THE BRAIN

The first arteriovenous aneurysm of the brain was reported by Steinheil¹⁰ in 1895, or 138 years after William Hunter's¹ first reported arteriovenous aneurysms in the arm.

A total of twenty-two cases which seemed to represent this type of intracranial aneurysm have been collected from the available records. Two additional cases of Struppler¹⁵ and Simmonds¹⁶ (second case) have

8. Krause, F.: *Chirurgie des Gehirns und Rückenmarks*, vol. 1, p. 88, 1908, English trans., New York, Rebman Company.

9. Astwazaturoff, M.: *Ueber die kavernöse Blutgeschwulst des Gehirns (zur Kasuistik der Pseudomeningitis)*, Frankfurt. Ztschr. f. Path., 1911, vol. 4.

10. Steinheil, S. O.: *Ueber einen Fall von Varix aneurysmaticus im Bereich der Gehirngefäße*, Inaug. Diss., Würzburg, 1895.

11. Kalischer, S.: *Demonstration des Gehirns eines Kindes mit Teleangiectasien der linksseitigen Gesichtskopfhaut und Hirnoberfläche*, Berl. klin. Wchnschr. 34:1059, 1897.

12. Mühsam, R.: *Ueber Varicen und Angiome des Zentralnervensystems*, Arch. f. klin. Chir. 130:522, 1924.

13. v. Eiselberg, A. F., and Ranzi, E.: *Ueber die chirurgische Behandlung der Hirn- und Rückenmarkstumoren. Ligatur von Angiomen*, Arch. f. klin. Chir. 102:341, 1913.

14. Campbell, H., and Ballance, C.: *Case of Venous Angioma of Cerebral Cortex*, Lancet 1:10, 1922.

15. Struppler: *Ueber das Cavernöse Angioma des Grosshirns*, München. med. Wchnschr. 37:1269, 1900.

16. Simmonds, M.: *Ueber das Angioma racemosum serpentinum des Gehirns*, Virchows Arch. f. path. Anat. 180:280, 1905.

and had complained of some stiffness in this arm. The attacks usually occurred in the early morning. He has had some trouble with his memory; he said that he often forgot most important things.

Examination.—A tenderness to deep pressure was revealed over the right parietal region. The patient said that there was a localized sore spot in this region (not over the tumor as later discovered). The neurologic examination did not reveal anything. The eyegrounds were normal. The roentgenogram of the head was negative. The Wassermann reaction of the blood was negative.

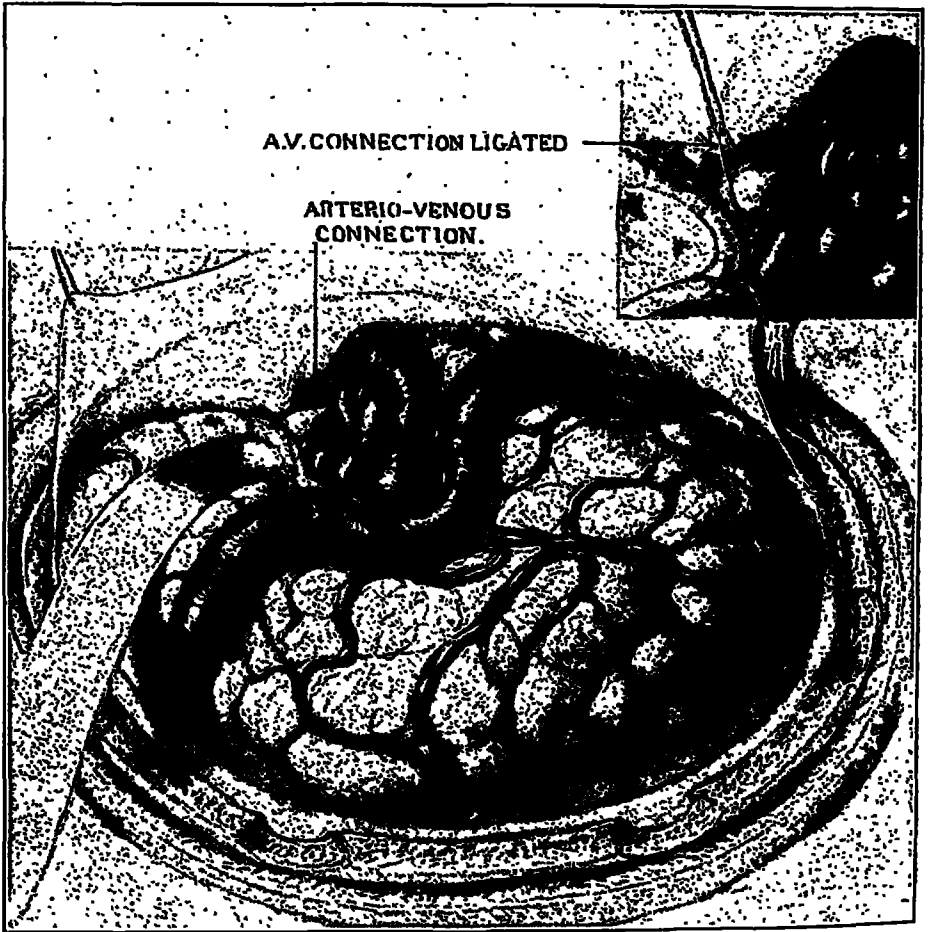


Fig. 2 (case 1).—An anomalous branch connecting the middle cerebral artery with the angiomatic mass. The transition from the artery to the vein is shown in the net work.

While he was in the hospital, an attack was observed by the nurse, but focal signs other than turning the head to the left were not seen. Urine was lost. Motor weakness did not follow the attack.

The injection of air into the cerebral ventricles showed dislocation of the ventricular system to the left side. The third ventricle was also bent obliquely to the left. The anterior horn of the right ventricle was smaller than the left. A diagnosis of right frontal tumor was made.

Operation.—Right craniotomy was performed. A group of tremendous engorged and tortuous veins covered the anterior half of the right temporal lobe, and to a much lesser extent the frontal lobe. They emptied into a huge sylvian

cent of the cases. It is clear that more cases will be disclosed at operation than at necropsy, because the symptoms (usually epilepsy) are not such as to require prolonged hospitalization. Most of the necropsies were obtained on patients who were brought to the hospital in coma resulting from cerebral hemorrhage. This number obviously represents but a small proportion of the afflicted persons.

CASES OF INTRACRANIAL ARTERIOVENOUS ANEURYSM

CASE 1.—History.—A well nourished, well built, muscular man, aged 52, an army officer, was suddenly and without warning seized with a severe clonic con-

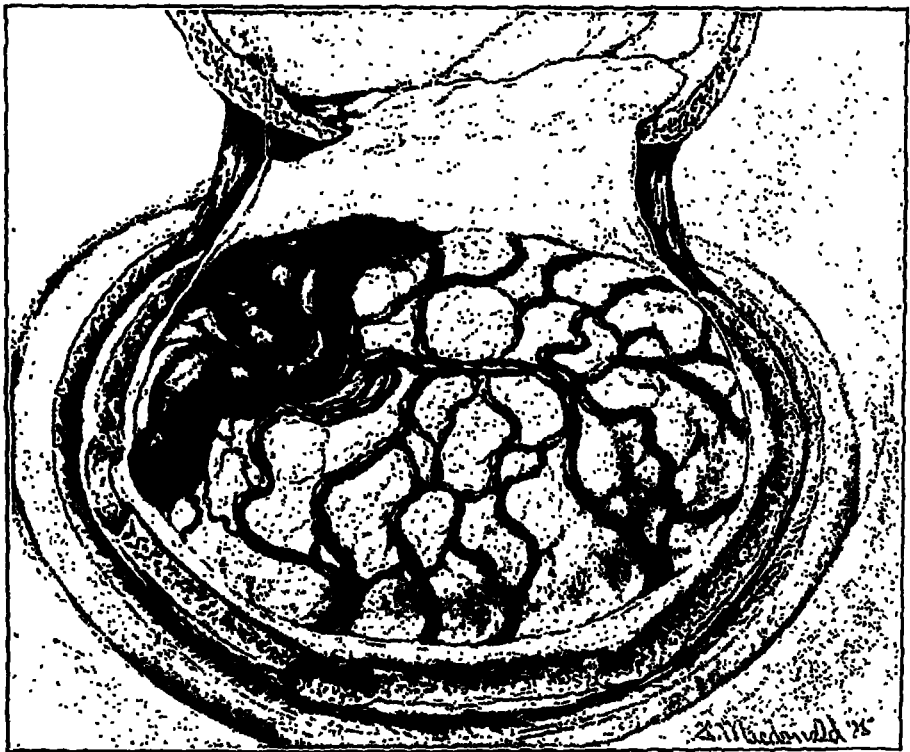


Fig. 1 (case 1).—Arteriovenous aneurysm showing a large sylvian vein emptying into the large anomalous vein crossing the temporal and frontal lobes. There is a distinct enlargement at the point of junction of these two veins; the rolandic vein is easily defined.

vulsion lasting about fifteen minutes. This attack occurred six years prior to examination, just after his return from France, where he actively participated in the World War. He had never had any kind of an attack before. For the next three years similar attacks occurred about once every two months; then for two years there was no attack, but for the past year they have appeared about every month. Recently, there have been petit mal attacks with loss of consciousness for from forty to sixty seconds, but no muscular contractions. One week ago he had a violent generalized headache; following this, a pain persisted in the right frontal region. His head turned to the left during the convulsions, but there was no other focal sign. At times he had had a dull aching pain in the fingers of the left hand

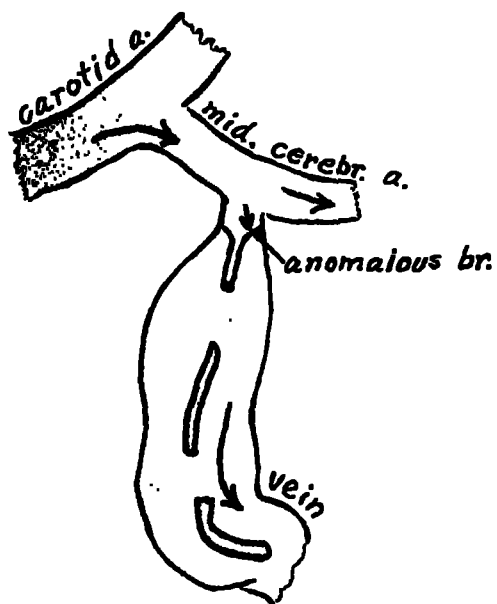


Fig. 3.—The direct communication between the artery and vein by means of an anomalous vessel.

was almost as large as the middle cerebral artery at this point. The arterial portion of the vessel was well isolated, surrounded by two silk sutures and ligated. The venous tumor immediately collapsed. We did not see any suggestion of a central tumor mass such as was present in other cases of the series from which the veins emerged. It was our impression that the condition was a pure arteriovenous fistula, produced by an anomalous vessel passing directly from the middle cerebral artery into a large venous trunk, which ultimately reached the sylvian vein. The great veins could be seen to connect with the sylvian vein.

Postoperative Course.—When the patient was coming out from under the effects of the ether, he complained of severe headache and weakness of the contralateral part of the arm and the leg. During the ensuing twenty-four hours, this side slowly became completely paralyzed, and his pulse rate steadily dropped to 60. Since the patient was somewhat drowsy, we suspected an extradural hemorrhage, but elevation of the bone flap did not show any collection of blood. The paralysis puzzled us, for our manipulations were entirely under the frontal lobe, too far afield from the motor tract to cause motor weakness, and seemingly remote from the middle cerebral artery. If the middle cerebral artery had by some chance been injured, why did the paralysis develop so gradually? We have also wondered whether the drop in the pulse rate might not be similar to the bradycardia noted by Holman as a constant sequel to the closure of arteriovenous fistulas in his series of dogs. Five days after the operation, recovery of function began in the left side and steadily progressed. Still unable to explain the cause of the hemiplegia, it is equally difficult to explain the recovery. Aside from a slight residual weakness of the left arm and hand and a slight limp, the patient was well three and a half years after the operation. Two and a half years after the operation, he had one convulsion; since then there have been no other seizures, either petit or grand mal, nor have there been any headaches or soreness corresponding to the old "localized tender spot." The spells of forgetfulness have disappeared.

CASE 2.—History.—A well nourished, normal looking boy, aged 19, sought relief from convulsions (1922). At the age of 15, he was seized with numbness in the left corner of his mouth. A "pricking sensation as of pins and needles" quickly followed and spread over the left side of the face. The tongue was pulled to the left, and it also had a similar "sensation as of pins and needles." The left side of the face twitched. The sensation spread to the left arm, but the arm did not twitch. The attack lasted only about one minute. The hand was weak for several minutes after the attack; consciousness was lost. Five months later, he was attacked by a convulsion while asleep. He foamed at the mouth, and urine was passed. During the following two months there were four more such attacks, all occurring during sleep, then a free interval of several months.

One year ago, a unilateral (left side) convulsion was not accompanied by loss of consciousness, and similar attacks have since occurred about once a month, always with the warning aura of numbness at the corner of the mouth. There has been only one unconscious spell during the past year; the hand and arm are always weak after such a spell.

Examination.—The results of the examination were negative. There was no objective evidence of motor weakness on the left side. The reflexes were normal and equal on the two sides. The roentgenogram was negative. The Wassermann reaction of the blood was negative. The preoperative diagnosis was probable cerebral tumor causing jacksonian epilepsy. A tumor was suspected because motor weakness followed in the wake of the convulsion.

Operation.—Feb. 11, 1922: Right craniotomy was performed. On the dural side of the bone flap, the inner table of the skull was eroded in a circular area

vein, joined at right angles a large anomalous vein which crossed the frontal lobe in a vertical direction and continued downward across the temporal lobe. There was no well defined rolandic vein. The network of veins dipped over the anterior margin of the temporal lobe, entirely obscuring the anterior pole. The largest venous trunk was over 1 cm. in diameter. The veins were a definite pink and were in striking contrast to the black veins elsewhere in the brain. One could easily see the blood rhythmically (with each heart beat) passing through the dilated thin walls of the veins. On palpation, a distinct thrill could be detected in the veins. Since any attempt to treat the aneurysm surgically appeared to involve a

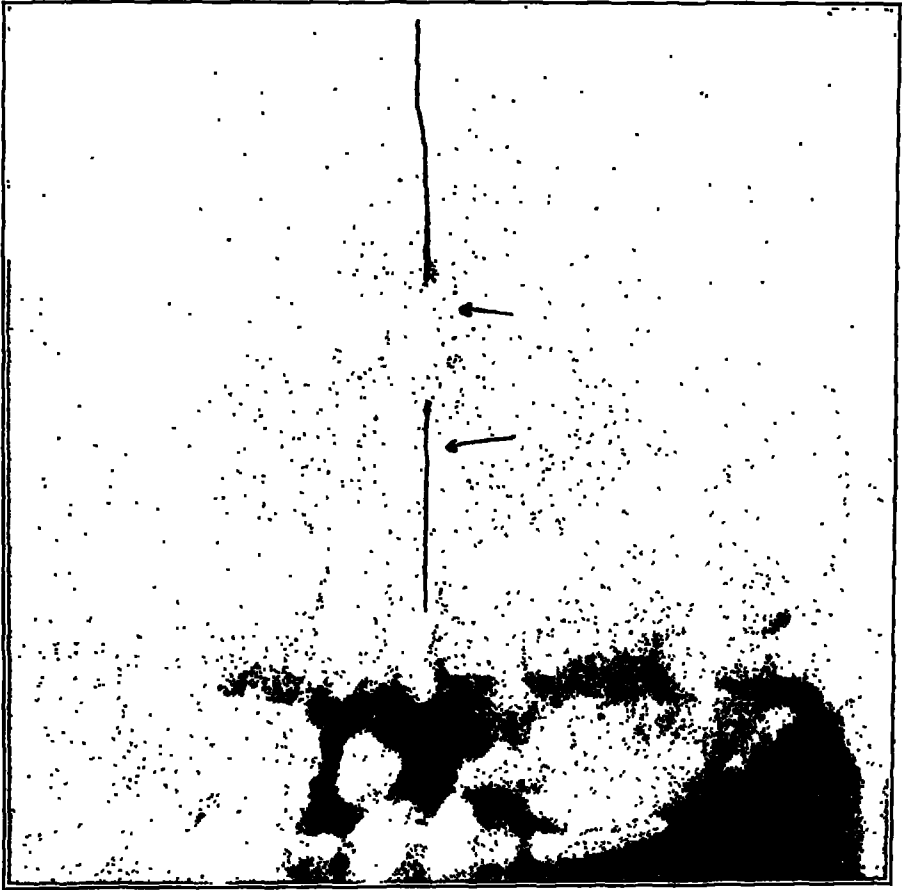


Fig. 4 (case 1).—Ventriculogram showing dislocation of the ventricles to the left and the deep third ventricle. The arrows indicate the dislocation of the ventricular system toward the left.

risk greater than my co-workers and I were justified in assuming, the dura was closed and the bone flap was replaced.

Second Operation.—Two weeks later the wound was reopened, the frontal lobe retracted and the inferior surface of the frontal lobe and the anterior pole of the temporal lobe well explored. Search was at once made for an arterial communication. A large anomalous branch passed from the middle cerebral artery (immediately distal to its origin) directly into the mass of engorged serpentine vessels. It was thick-walled and definitely arterial at its origin, but less than 0.5 cm. distally there was an abrupt transition to a thin-walled vein. This vessel

After consultation with the patient's brother, who realized the great danger involved, an attempt was made to extirpate the mass. It was hoped that the surface vessels might be ligated and the tumor undermined and included in a mass dissection of brain tissue, without actually coming in contact with the vessels of the tumor. As this was our first experience with this type of lesion, we little realized its extreme difficulties and dangers. The sylvian vein was tied with two silk ligatures and the vessel divided. We hoped to work through the cortex from this point mesially, but as there was not sufficient room, the line of attack was shifted to the mesial aspect of the tumor. The rolandic vein was doubly tied and divided. A remarkable resistance was encountered in ligating the vein. Usually a vein offers almost no resistance to the sliding knot, but in this instance the knot could be slipped down only step by step because of the pressure within the vein. Ligation and division of the rolandic vein were accomplished without incident. A few minutes later, however, while a subcortical dissection was being performed and preparation was being made to ligate additional vessels, a sudden burst of blood flooded the operative field. The rolandic vein had burst, not at the points of ligation but in the bulge of the vein about midway between the ligatures on its now isolated segment. The closure of the venous outlets had taken away too many of the channels of exit for blood from the tumor and the thin-walled rolandic vein, no longer able to withstand the added extra strain of increasing arterial pressure, burst at its weakest point. The bleeding became profuse. Pressure with cotton and gauze accomplished little more than to check the bleeding temporarily. A rapid extirpation of the mass was attempted, but the bleeding vessels multiplied. There was no cerebral tissue, only a skein of wormlike vessels which bled furiously. The carotid vein was tied in the neck, and while this reduced the bleeding so that tampons of cotton controlled it, shortly afterward the renewed pressure established by collateral again lifted the cotton pack, and the bleeding began anew. When it was again stopped, the patient's condition was so seriously affected that he died a few hours later.

CASE 3.—History.—A healthy looking man, aged 35, was referred by Dr. Ralph Greene, of Jacksonville, Fla., on Jan. 25, 1925, because of a general mental and physical breakdown, headache, double vision, periods of somnolence, slurring speech and staggering gait.

The patient's condition was said to have begun two years before examination with a staggering gait and a tendency to swerve to the left. He said that he would fall to the left any time when his eyes were shut. Diplopia had been present more or less continually for the past two years. Dizziness was frequent and disturbing. A thick slurring speech had been noticed for a month. Headaches had occurred irregularly, but were more noticeable when the patient was constipated. There was also pronounced mental impairment with paranoid trend. He was irritable and suspicious and adopted a superior attitude. His insight and judgment were poor. His speech was slurring and he quickly rambled over a number of subjects without cohesion and without meaning. He had formerly studied medicine and apparently did well until he stopped because of a dislike for the subject. His memory was uncertain. Convulsions, loss of consciousness, motor or sensory disturbances or difficulty in swallowing were not noted.

Examination.—The neurologic examination showed bilateral choked disk of 3 diopters in each eye. There were no obvious extra-ocular palsies to explain diplopia; coarse nystagmoid jerks of the eyeballs occurred when the patient looked far to the right or left. There was dysarthria; greatly diminished hearing in the left ear; slight ataxia in the heel to knee test, but not in the finger to nose

test; staggering gait; positive Romberg sign, the patient falling constantly to the left and no adiadokokinesis. He walked with a broad base.

There were bilateral positive Babinski and Oppenheim signs; otherwise the reflexes were normal. There were no motor or sensory changes. The Wassermann test of the blood was negative. A roentgenogram of the head was negative.

A tentative diagnosis of cerebellar tumor was made, but the pronounced mental changes were unexplainable.

Ventricular estimation showed both ventricles to be large and in free communication with each other (indigo-carmin test). The fluid was under greatly increased pressure.

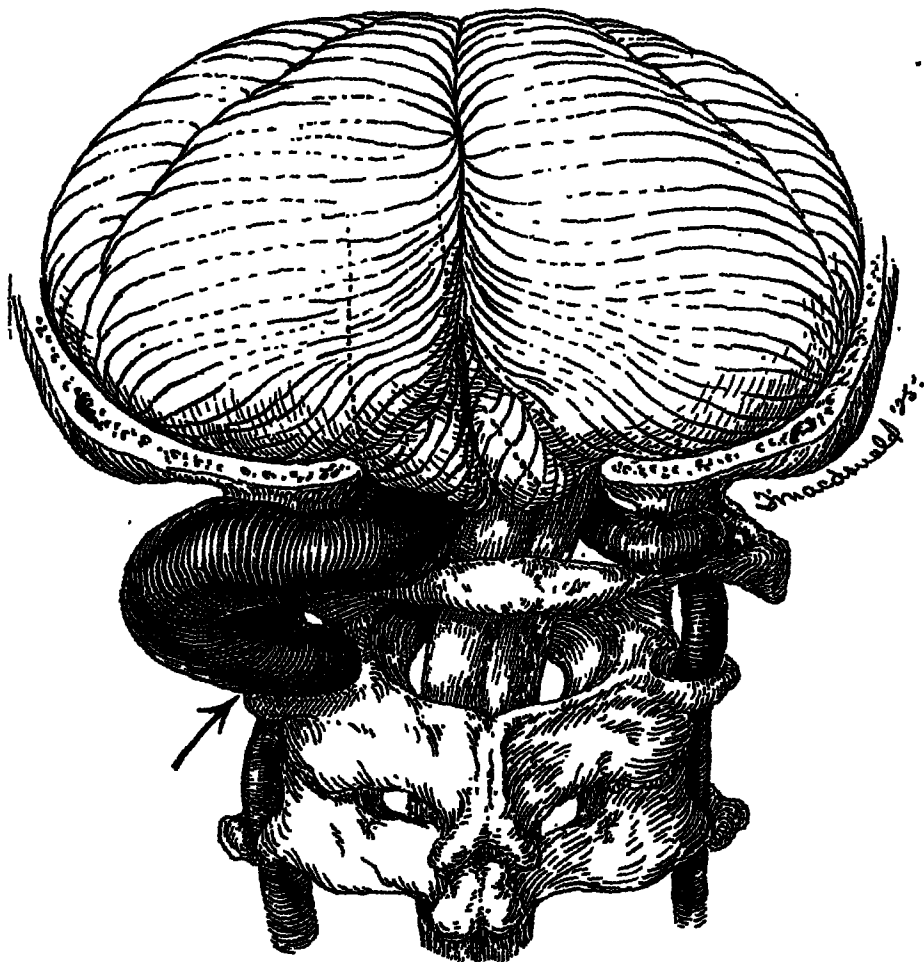


Fig. 8 (case 3).—Sketch of aneurysm showing the tremendous vertebral artery on this side. This diagrammatic sketch is intended to show the difference between the vertebral arteries on the two sides. The sketch is not accurate in that the bulge of the artery was between the atlas and the axis, but from the artist's view at the operation it might well have looked as it does. The artery was doubtless also enlarged below this point, though it could not be inspected at the operation.

Operation.—A cerebellar exploratory operation was performed. When the cerebellum was exposed, six large tortuous veins stood out in strong relief about equally on both cerebellar lobes. They converged to two large trunks at the border of the superior surface and dipped out of sight onto the tentorial surface

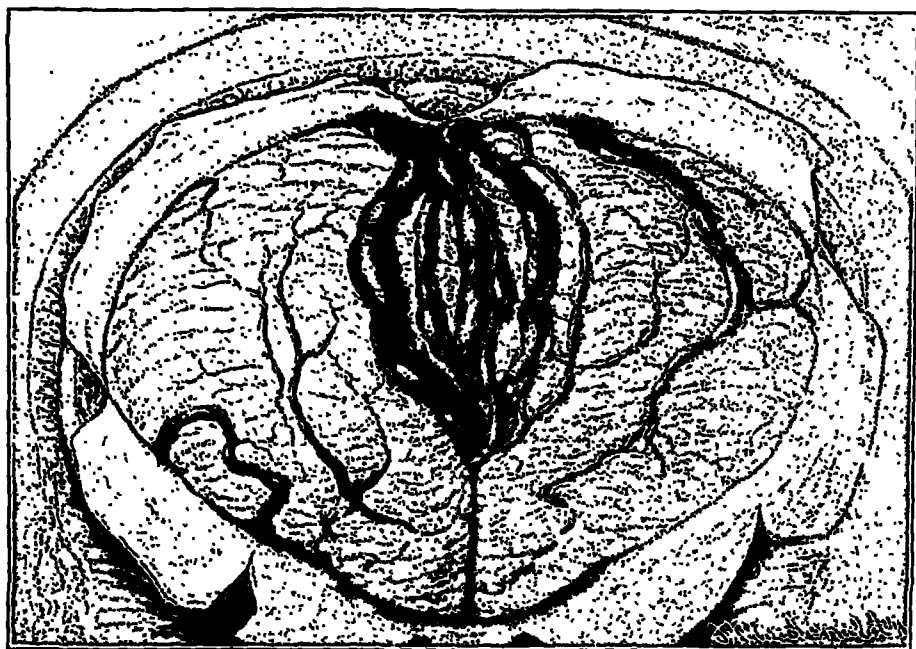


Fig. 6 (case 3).—Arteriovenous aneurysm in the posterior cranial fossa. The large veins on the surface of the cerebellum were lost under the dura.

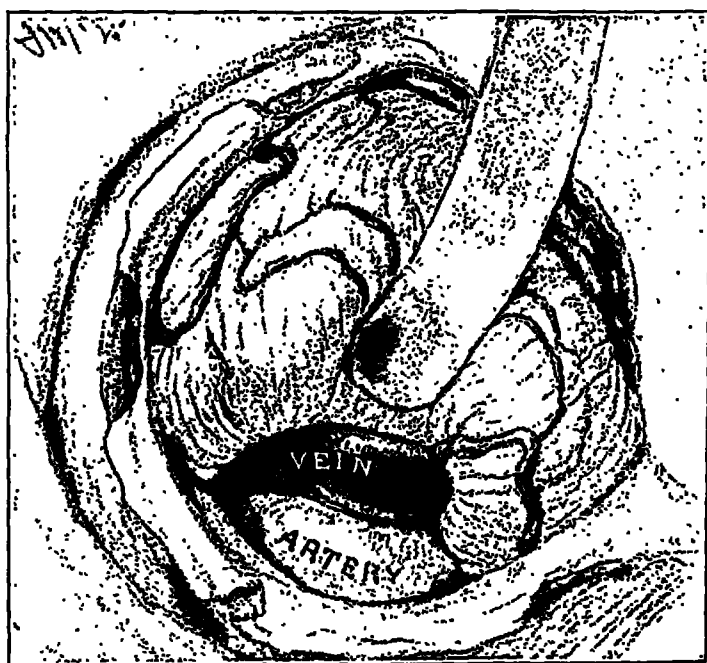


Fig. 7 (case 3).—Elevation of the left lobe of the cerebellum shows the big venous bed underlying and the tremendous vertebral artery beneath the vein.

wound was bulging and tight; immediately afterward it became soft and somewhat sunken, and remained so during the remainder of the patient's stay of a month in the hospital. A discharge note by Dr. Deryl Hart states that the bruit, formerly heard so strongly over both temples, could be heard only over the right (contralateral) temple. The gait was much improved; the Romberg, Babinski and Oppenheim signs were negative. Subjective diplopia still persisted.

Two and a half years later, the patient wrote that he had remained well and free from headaches, but, judging by his letter, there had not been any mental improvement.

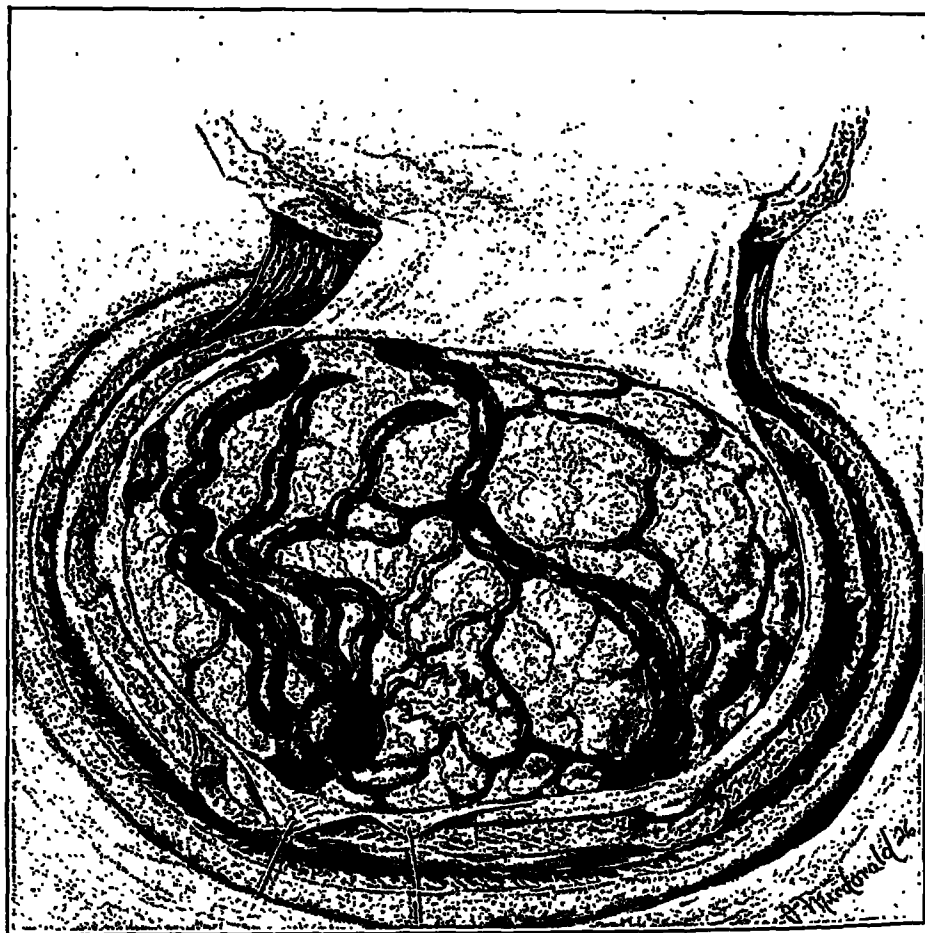


Fig. 10 (case 4).—A spider-like arrangement of veins abnormal in both size and position are directed toward the central swelling, which is just above and underlying beneath, and which can be palpated.

CASE 4.—History.—A sparely nourished man, aged 47, was referred by Dr. L. E. Stubbs and Dr. H. W. Curtis, of Newport News, Va., on Oct. 1, 1925, because of frequent jacksonian convulsions and some motor weakness. Six years before this, he was suddenly seized with a cramp in the left hand; this was immediately followed by weakness of the legs, loss of consciousness and a convulsion. He regained consciousness an hour and ten minutes later, but was so weak that he could not leave the bed for three days. A month later, he was seized with an attack similar in origin but less severe; consciousness was lost for only a few minutes. During the next three years, such attacks occurred with fair regularity

Examination.—The neurologic examination showed that there was some motor weakness of the left side of the face and of the left arm, but not of the leg. Sensation was not changed. Biceps and triceps reflexes were markedly increased on the left side. The knee jerks were slightly greater on the left; the Babinski sign was negative. The Wassermann reaction of the blood was negative.

A roentgenogram of the head showed a group of calcified areas in the right frontoparietal region. In the anteroposterior view, these extended almost from the surface to the midline. The shadows were linear and circular, and in one place there was a definite whorl. The shape of these shadows suggested a vascular pattern, and from the roentgen-ray observations alone, a vascular tumor was suspected.



Fig. 12 (case 4).—Patient after the cerebral exploration and after the ligation of the internal carotid artery on the affected side. The partial occlusion later became complete by the reaction around the rubber band which was used to restrict it.

Operation.—On Oct. 3, 1925, a left craniotomy was performed over the region so clearly defined in the roentgenograms. The inner table of the bone was much thinner. These changes of pressure were due to a localized dilatation along the course of a large tortuous cerebral vein in front of and below the face portion of the Rolandic area. From this venous center four large tortuous veins radiated as from the hub of a wheel (fig. 10). This venous dilatation was also situated almost in the center of an indurated subcortical mass, sharply defined by palpation and measuring about 5 by 5 cm. The large venous dilatation could be seen to pulsate, and when partially obliterated a thrill was imparted to the palpating finger. At each heart beat, the swirling red (arterial) blood could be seen through the walls of the vein. There seemed no hope of a successful

about every two months. Three years before coming to Dr. Stubbs and Dr. Curtis, he had the first attack in which he was conscious throughout. A cramp attacked the left hand, causing his hand to close into a fist; the arm quickly became rigid and drew up above the head. He had a sensation of being unable to catch his breath; he thought it grew dark about him, and it seemed as if his heart had stopped beating; profuse perspiration broke out. He thought he was going to die. He thought his left leg was paralyzed, for he could not move it; the muscles of his trunk did not seem to be affected. This attack lasted half an hour, gradually passing away. For the next two years, there were no

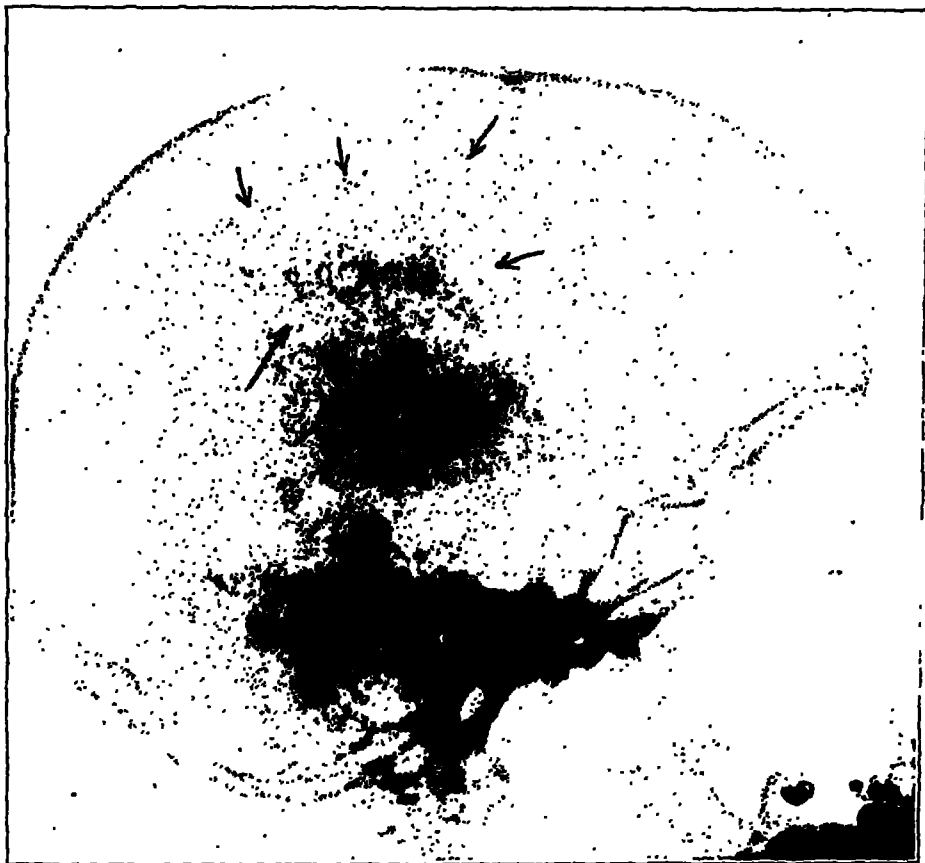


Fig. 11 (case 4).—Roentgen-ray observations. The arrows are directed toward the enormous shadows, and the whorl-like calcification of the vessel in the aneurysm is the most conspicuous shadow in the group.

more attacks (he was taking phenobarbital); then followed an attack like the last one. Since then similar attacks, without loss of consciousness, had occurred at intervals of about two months. After one attack the left arm and leg were paralyzed for half an hour, the function gradually returning. In addition, the left arm steadily became weaker, until it was considerably disabled. There had been only one attack at night, and no petit mal attacks. Severe headaches occurred after the attacks; with these exceptions, he did not have headaches. The attacks appeared to be induced by constipation, but not by exercise or excitement. Phenobarbital was definitely helpful; he ascribed the two years' free interval from attacks to this drug. There was no history of trauma.

A ventriculography showed that in the right postrolandic region there was a great defect which was in free communication with the body of the lateral ventricle. The loss of cerebral tissue was interpreted to be the sequel of the hemorrhage which had occurred seven months before. The actual tumor or aneurysm did not show, but was assumed to be alongside the cerebral defect.

Operation.—On July 21, 1925, a right craniotomy was performed. A plexus of large, tortuous veins obscured the brain just above the sylvian vein and below and posterior to the motor face area. The rolandic vein, which skirted the mass of superficial veins, was two or three times its normal size; the sylvian vein was also much enlarged. This circumscribed mass of veins dipped

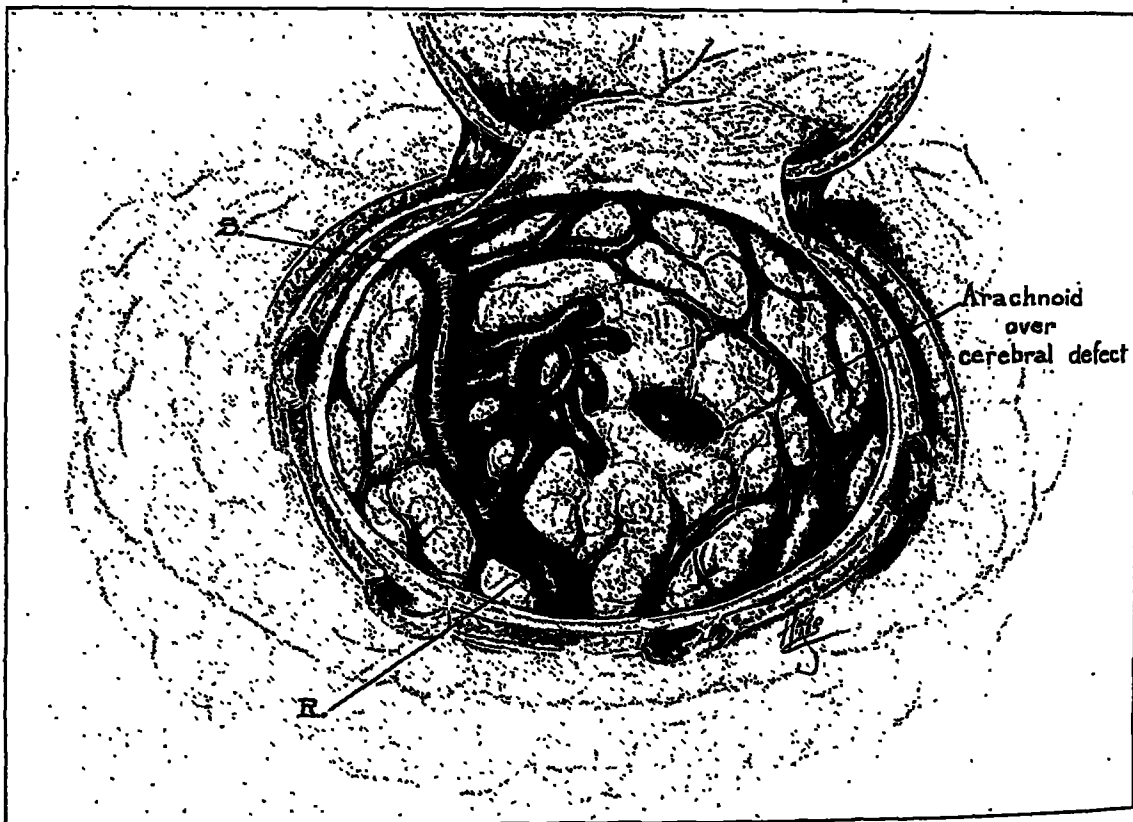


Fig. 13 (case 5).—The cluster of veins overlying and draining the mass of vessels below the surface of the vein. These veins abnormal in position empty into the tremendous rolandic vein which is continuous with an equally large sylvian vein. Arterial blood could clearly be seen in the veins. The cyst just posterior to the cluster of veins is the outer part of the defect which resulted from the cerebral hemorrhage which occurred several months previously.

into the cerebral cortex. Red arterial blood could be seen swirling in the rolandic vein with each heart beat. A thrill could not be felt.

About 1 cm. behind the venous plexus the meninges were transparent in an oval area about 1 by 1.5 cm. A cystlike dome was bulging upward from below. When this was opened, it proved to be the big ventricular dilatation (cerebral defect) indicated by the ventriculograms. The cerebral defect became larger below the surface and was nearly as large as a hen's egg. Its size was little reduced where it opened into the lateral ventricle.

surgical intervention for such a vicious arteriovenous lesion. A subtemporal decompression was made; it remained fairly full and tight after the operation.

Second Operation.—Three weeks later, it was decided to ligate the right common carotid artery. Because of the danger of this procedure at the patient's age, a partial occlusion was first made with a rubber band. Twelve days later, the wound was reopened, the artery was ligated above and below the band, and the intervening tissue (including the band) was excised. There was a rather extensive reaction of all the tissues contiguous to the rubber foreign body. The carotid artery was already completely occluded with firm fibrous tissue within its lumen. It was our impression at the time that this was a satisfactory method of inducing a gradual occlusion of the carotid. It would, however, be dangerous if eventual total occlusion of the internal carotid artery could not be tolerated. No untoward symptoms were noted at the time of partial ligation or subsequently when it became total.

When the carotid artery was exposed for ligation, a lumbar puncture was performed, and the height of spinal fluid was measured. On each temporary closure of the carotid artery (to test for possible symptoms of cerebral anemia), the spinal pressure became reduced from 280 to 255 mm. and returned to the previous normal level when the lumen of the carotid artery was again restored. The blood pressure rose from 168 to 175 each time the carotid artery was closed.

For five days after the operation, the decompression was markedly sunken, then becoming flush with the skin.

The convulsions disappeared for more than a year. They then returned in mild form, but after eighteen months had again become like the former attacks.

CASE 5.—History.—A well nourished man, aged 48, was first seen in coma in the medical service of the Johns Hopkins Hospital, on Jan. 21, 1925. During the past ten years, he had had four convulsive seizures with loss of consciousness and with involvement of the left arm and leg. He did not rouse from the attack he had just before his admission to the hospital. He had incontinence of urine and feces, a pulse rate of 44 and rapid, stertorous breathing. Gradually, the coma disappeared. A residual partial hemianesthesia, hemiplegia and homonymous hemianopsia were present on the left side when consciousness was restored. Eventually, all of these signs disappeared almost entirely. Bloody fluid was obtained from several lumbar punctures. He convalesced slowly, and when discharged from the hospital six weeks after the onset of coma, he was mentally confused and forgetful. There was no history of trauma.

Six months later (July, 1925), he had another attack, with unconsciousness, but it lasted only three or four minutes. Shortly afterward, he returned to the hospital for treatment. During the time since his comatose spell he had done some work, but had been morose and gloomy. After dinner he sat alone or went to bed, always shunning company. He was forgetful and at times confused.

Examination.—A slight homonymous defect was found in the left visual field; the left knee jerk was obtained only on reinforcement; the right, not at all. No motor or sensory disturbance remained on the left side. The blood pressure was 125 systolic and 85 diastolic. The Wassermann reaction of the blood was negative.

It was evident that the patient had had a cerebral hemorrhage in the parieto-occipital region. At his age, and with negative vascular signs, it was safe to assume the existence of an underlying tumor or aneurysm from which the hemorrhage had arisen.

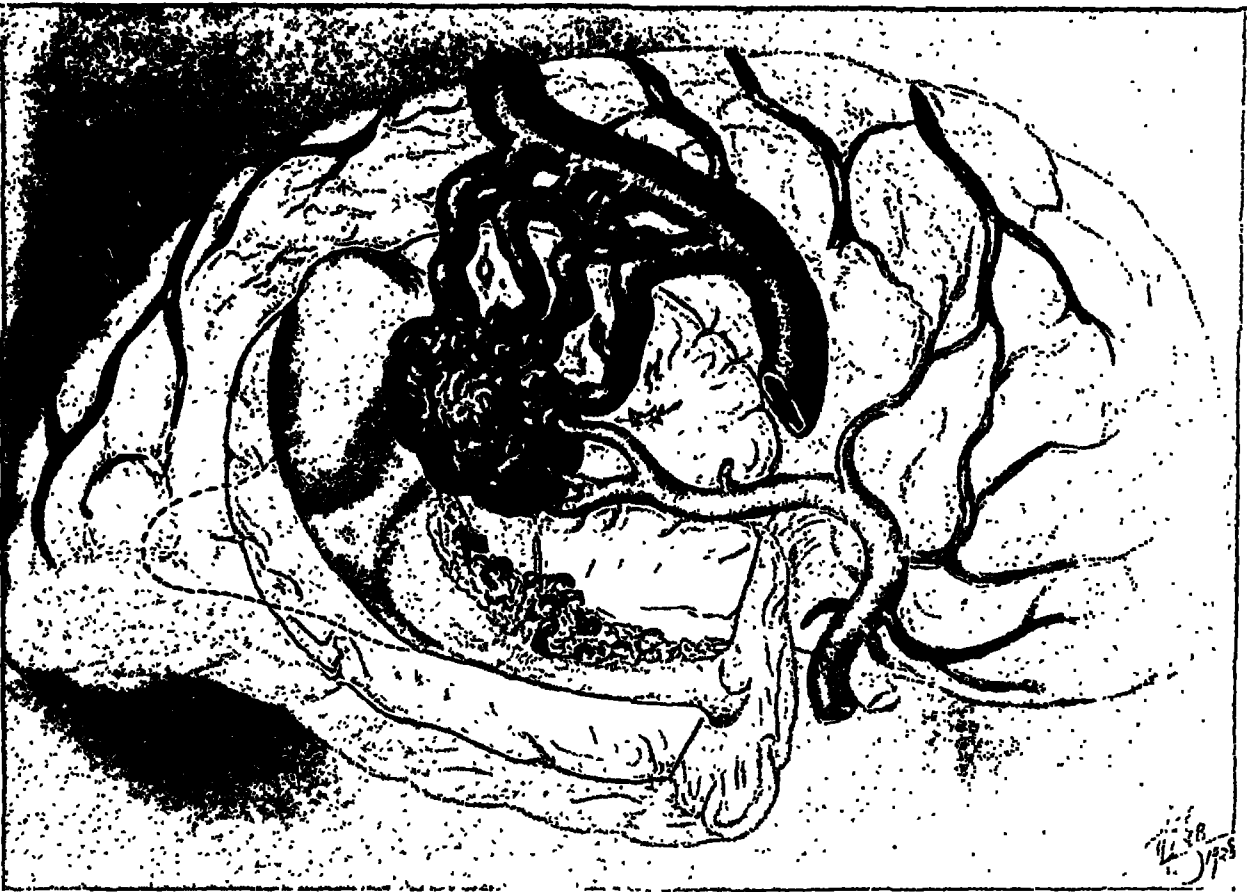


Fig. 14 (case 5).—Reconstruction of arteriovenous aneurysm from the necropsy specimen. The large middle cerebral artery terminates in the mass of vessels—the so-called angioma—whereas on the opposite side the middle meningeal artery continues on posteriorly. The vascular bed protrudes into the defect which has resulted from the cerebral hemorrhage and which communicates freely with the lateral ventricle.



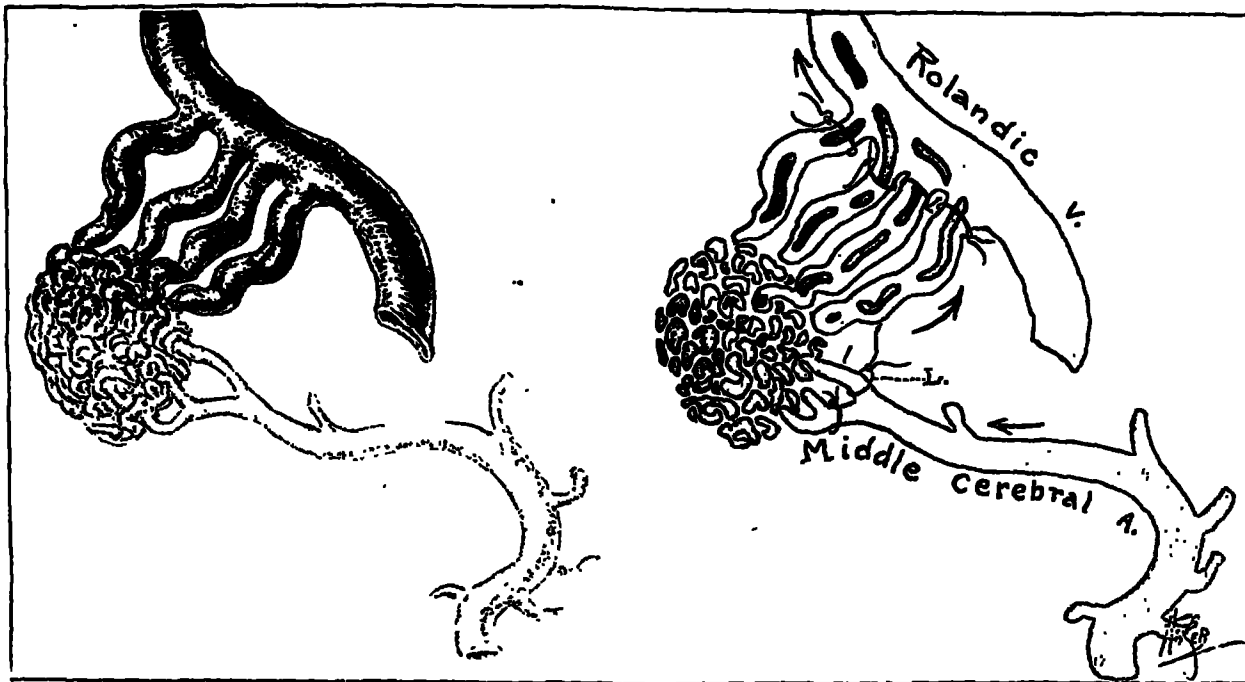


Fig. 15.—Diagram to show the construction and vascular arrangement of the arteriovenous aneurysm (case V, fig. 14). The vascular intracranial mass takes the place of the former capillary bed from which it doubtless is a congenital maldevelopment.

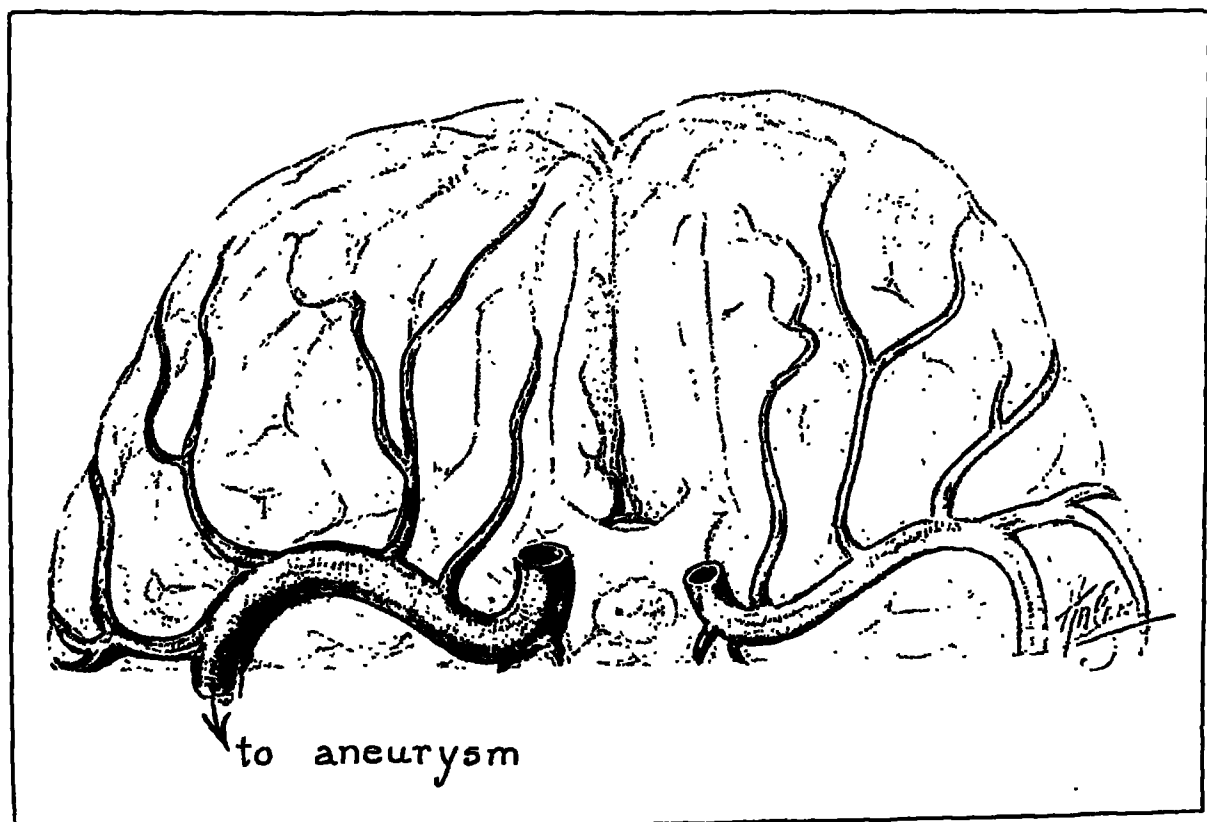


Fig. 16.—Sketch to show the relative size of the middle cerebral arteries on the normal and affected sides. The artery on the side of the aneurysm is considerably larger all the way to its origin in the carotid.

open ventricular system, this patient would surely have survived, for the hemorrhage would have been far less significant and easily handled. Our reasons for excising this tumor were: 1. The tumor was back of the rolandic area, and a hemiparesis could probably be avoided. 2. Owing to the protrusion of the arterial units into the cerebral defect, a cerebral hemorrhage would probably occur again and by flooding the ventricular system cause death.

The middle cerebral arteries of both sides were dissected after death. The right was from one-third to one-half larger, even to its origin at the carotid



Fig. 18 (case 5).—Ventriculogram of the affected side. The large shadow is the cerebral defect which has resulted from the old hemorrhage. It will be noted that the volume of air which filled the left ventricle was only enough to fill the defect in the right ventricle.

artery. The affected middle cerebral artery turned upward and terminated in the branches which entered the nest of vessels. The left artery, however, took an entirely different course in this region and for some distance continued backward toward the occipital lobe.

CASE 6.—History.—A well nourished young man, aged 31, complained of loss of vision, progressive weakness of the left arm and leg, headache and convulsions.

The first symptoms of onset, dating back fifteen years, were intermittent spells of blurred vision and headache across the forehead on the right side. These

In the anterior wall of the defect, several small, hard, dark gray nodules, from about 1 to 2 mm. in diameter, protruded into the cavity. Poorly covered by the white matter of the brain, they were recognized as vascular buds and as the outposts of a vascular tumor. Extirpation of the mass seemed possible and was attempted after ligation of the vessels on the surface of the brain. We were not unmindful of our earlier tragic experience in ligating the superficial veins, but this tumor looked far less vicious from the surface. After the tumor was circumvented by ligatures, extirpation was begun from the cyst forward. The cortex was first incised below the tumor in order to get the entering arterial trunks.

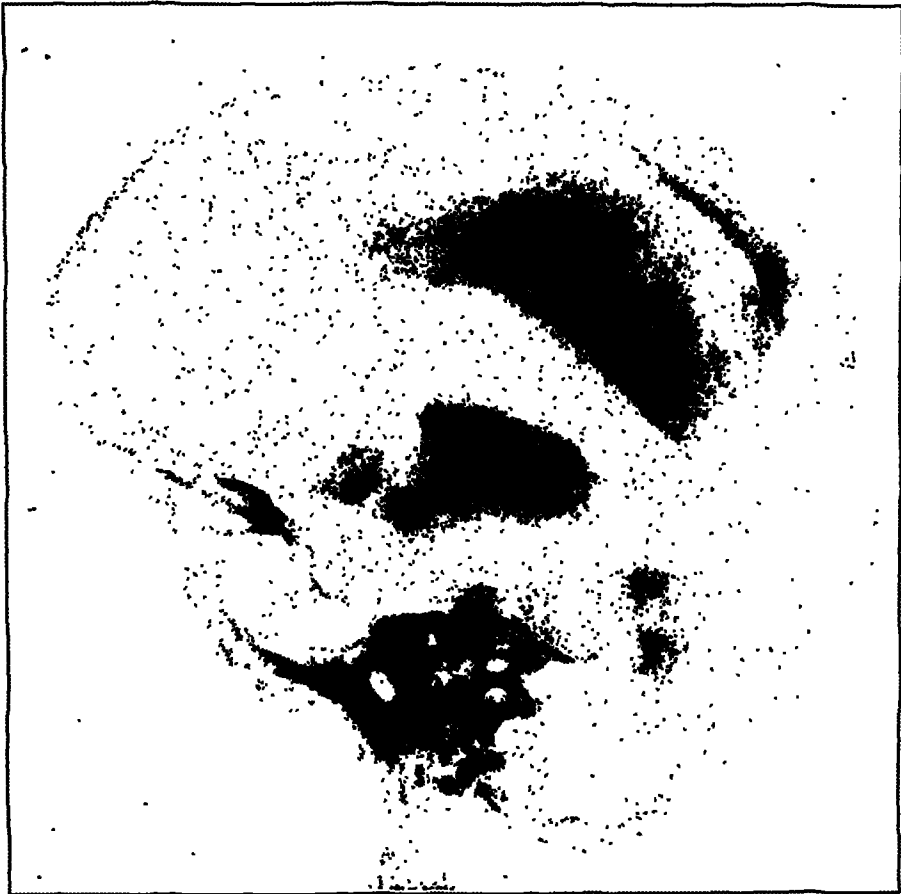


Fig. 17 (case 5).—Ventriculogram; a lateral view of the normal side.

A dense mass of intertwined serpentine red vessels of more uniform size was encountered.

A detour of the incision was made downward, and in this way the vascular mass was divided. Three fair-sized arteries were isolated near their entrance into the cluster of vessels. After ligation of the arterial supply, the vascular tumor was removed without difficulty. Bleeding was entirely stopped when closure was begun. However, despite a prompt recovery from the anesthetic, the patient died six days after the operation from a slowly developing intraventricular hemorrhage. During the operation the opening into the lateral ventricle had been carefully packed to preclude bleeding into it.

Necropsy showed three branches of the left middle cerebral artery clipped at the margin from which the tumor had been excised. Had it not been for the

Epileptic attacks appeared soon after the sensory and motor symptoms. They were initiated with numbness in the left arm and leg and a drawing sensation in the left side of the face, but consciousness was not lost. The attacks usually came while he was asleep and awakened him. A painful headache always followed. In some of the attacks, only part of the left side was involved. The epileptic attacks steadily increased from two or three a month in 1920 to fifteen a month. The later attacks began with numbness and stiffness of the fingers of the left hand and the toes of the left foot. The right side was never involved. Diplopia appeared recently. During the past three years the vessels over his face and head, particularly on the right side, have become much larger and more conspicuous.

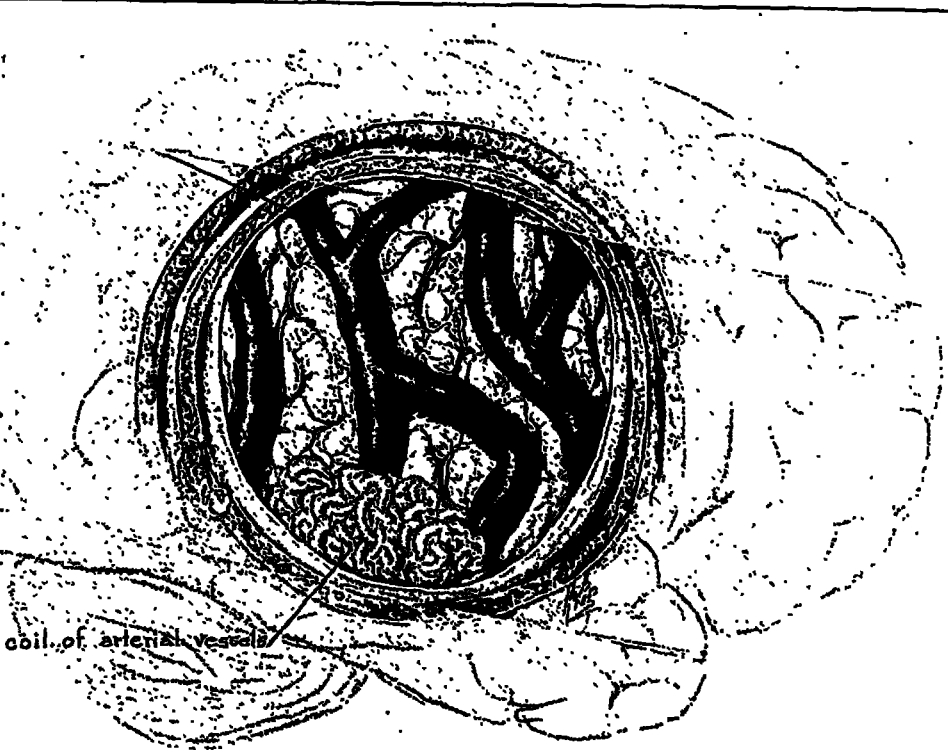


Fig. 20 (case 6).—Drawing of aneurysm as seen at operation. The interlacing vessels in the subdural space are clearly arterial. The large veins on the cortex of the brain drain the lesion which has doubtless extended into the brain.

Examination.—Over the occipital region of the right side was a diffuse bulging mass about 5 by 5 cm. but without sharply defined boundaries; it pulsed strongly with each heart beat. The superficial temporal, posterior auricular and occipital arteries were tortuous, much enlarged and easily visible. When all three of the arteries were compressed, the swelling in the scalp subsided and ceased to pulsate. A bony opening could be palpated just mesial to the right mastoid process and in the normal position of the mastoid vein. This opening, which also showed clearly in the roentgenogram, was about 1 by 1 cm. in diameter. Another small opening in the right frontal region was all that remained of a gradually closing decompression (performed ten years before). When the patient stooped, the veins

spells occurred once or twice a week. Limitation of vision to either side was not noticed at that time. In 1916, a decompression and puncture of the corpus callosum were performed at the Mayo Clinic. The patient was benefited for a short time, but the symptoms gradually returned.

In 1918, while on duty in France, he fell from a horse; a severe headache developed, but lasted only for several days. Craniotomy was performed at the Mayo Clinic in 1920. At that time, a choked disk was reported, and at the opera-



Fig. 19 (case 5).—Low power microscopic view of the network of vessels in the so-called angioma. These vessels vary tremendously in size and in the thickness of their walls, some contain elastic tissue of irregular strands; others do not. There is much thrombosis and irregular thickening of the intima.

tion, unusually large cortical vessels were noted. For the past six years, he has steadily become worse. His vision has steadily diminished; since 1920, he has been unable to see to the left side (left homonymous hemianopsia). The sense of pressure in the head, and particularly in the right temple, has become more and more intense. Numbness and weakness in the left hand, arm and leg began about 1921, and have gradually increased.

vein, a vein of corresponding size entered, filling the opening, and carried the blood from the vascular tumor. The angioma was dissected from the scalp and its entering arteries carefully marked for later study. The huge vein was carefully ligated at the bony opening with a transfixion suture of silk. Immediately after the operation, each vessel was carefully traced. The occipital artery passed directly into the big mastoid vein. This continuity was demonstrable by a probe which passed without interruption from the artery into the vein. Likewise a probe in the posterior auricular artery passed directly into the occipital artery just before it entered the big mastoid vein. A third small artery; presumably a branch of the superficial temporal, could not be traced accurately. There was, therefore, an arteriovenous fistula between the occipital artery and the mastoid vein and another interarterial fistula between the posterior auricular and the occipital arteries. The position of the great mastoid vein suggested that it entered the lateral venous sinus; it, therefore, seemed probable that the external arteriovenous fistula was separate and distinct from the arteriovenous aneurysm within the cranial chamber. Whether they were in communication through the lateral sinus could not be determined.

Second Operation.—July 20, 1926: The patient's signs and symptoms had been unchanged after the external operation. Feeling that an attack on the intracranial aneurysm would be too hazardous, a large right subtemporal decompression was performed in order to relieve the intracranial pressure. It was hoped that the patient might be relieved, at least to the extent of stopping the headaches and preserving the vision which was being menaced by a high papilledema.

When the dura, which was excessively bloody, was cautiously opened, several tortuous vessels lying in the subdural space were found attached to the inner side of the dura. Most of these vessels could be stripped away from the dura, but others entered it and had to be ligated. These extremely tortuous vessels were red and pulsated strongly. All that were visible were clearly arterial channels.

These arteries, which formed free loops in the subdural space, could be compared only to a tangled mass of angle worms; they were also about that size and fairly uniform. This vascular tumor was situated along the posterior part of the temporal lobe. Everywhere this part of the brain was completely hidden from view. Three tremendous veins emerged from this cluster of vessels. A fourth vein of about the same size paralleled the anterior part of the decompression and could not be seen to enter the angioma. Pulsation could be seen and a thrill palpated in these veins.

When the vessels were freed from the dura, furious bleeding resulted. It was possible to control the hemorrhage only by a cotton pack. The next day, careful removal of the pack was again followed by arterial bleeding, though somewhat less severe. A piece of muscle then controlled it.

The headaches were entirely relieved by the operation, but the symptoms and signs have remained as before. The decompression has since bulged at times, but at other times has been sunken.

CASE 7.—History.—A normal looking boy, aged 14, was referred by Dr. Ralph Greene, of Jacksonville, Fla., because of jacksonian epilepsy (Oct. 27, 1926). His trouble dated back to the age of 7 years, when his mother handed him a glass of water; he dropped it and said his hand was weak and that he could not hold it. He was conscious throughout the attack. A few weeks later when cutting paper, he complained that he could not use his right hand. Three months later, when at school, he had the first convulsion. After the attack, he recalled that his tongue

of the head and face became enormous. A loud systolic murmur was heard over the entire head, but much more over the right parietal and occipital regions.

The positive neurologic observations were: high grade papilledema (6 diopters) in both fundi; hypesthesia for pain, touch and temperature over the left side of the face and of the left arm and leg; slight weakness of the left facial muscles. The patient walked with a decidedly spastic hemiplegia gait; the left hand and arm were weaker than the right; sharply defined and complete left homonymous hemianopsia was present.

The corneal reflex was less active on the left; the knee jerks, biceps, triceps and achilles reflexes were exaggerated on the left; there was ankle clonus on the left; the Babinski sign was negative.

A roentgenogram showed a circular opening (1 by 1 cm.) in the occipital bone just mesial to the right mastoid process.

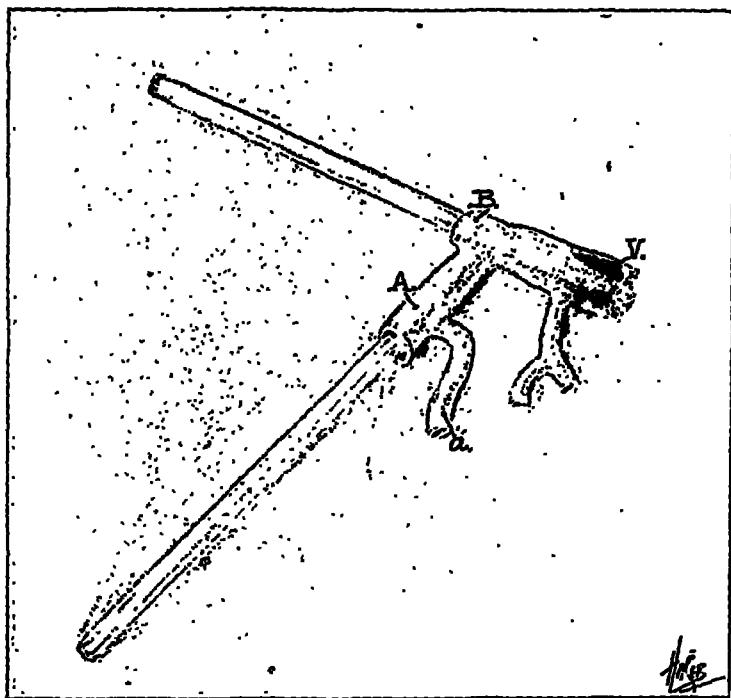


Fig. 21 (case 6).—Arteriovenous aneurysm of the scalp. The upper glass rod passes from the occipital artery into the mastoid vein (*V*). The posterior auricular artery (*A*) also is seen passing into the occipital artery near its junction with the mastoid vein. The mastoid vein entered a hole as large as one's finger to the left of the mastoid process. The superficial temporal artery (?) enters at the line of communication between the artery and veins.

Operation.—June 20, 1926: Since the extensive pulsating mass in the left occiput seemed to be dependent on the patency of the superficial temporal, the posterior auricular and the vertebral arteries, these were first ligated, although it was evident that the intracranial lesion (presumably also an arteriovenous aneurysm) was much more extensive, since there was hemianopsia, partial hemianesthesia and hemiplegia. The mass of vessels in the scalp was carefully dissected, and at the time the branches of the external carotid artery were exposed for ligation. All three of the vessels entered the extracranial vascular mass, and through the large, bony opening which corresponded in position to the mastoid

A diagnosis of tumor or aneurysm was made, more probably the latter because of the old history of a cerebral hemorrhage and with so little progression of signs or symptoms over a period of seven years.

A filling defect nearly obliterated the anterior part of the body of the left lateral ventricle. In the background of air, a linear calcified shadow was clearly visible, whereas in the roentgenogram without air, this shadow could not be seen.

Operation.—On Oct. 29, 1926, left craniotomy was performed. When the dura was exposed, a localized bluish swelling was evident toward the mesial part of the bony defect. The dura over this region had been unusually bloody; it was also thinner than elsewhere. The localized bulge was due to an underlying venous dilatation which appeared to come out of the brain tissue and which passed into a large vein that coursed mesially to the superior longitudinal sinus. It corresponded in position with the rolandic vein, which it undoubtedly represented. A second smaller vein passed downward from the mass to the sylvian vein. The large rolandic vein was distinctly red, and through its thin walls the pulsing red blood could be seen rhythmically mixing with the darker venous blood. No other enlarged veins were present on the surface of the brain. Palpation of the brain revealed an indurated area beneath the face area, but no attempt was made to expose the underlying tumor or to treat the lesion in any way. Its position in the important part of the leading cerebral hemisphere precluded any further effort.

A year later, his condition was practically unchanged.

CASE 8.—History.—A well nourished man, aged 35, in good general health, complained of generalized convulsions (May 5, 1925). His first attack had occurred fourteen months earlier. It was described as a generalized convulsion which came without warning and lasted about half an hour. He frothed at the mouth, bit his tongue but did not have incontinence of urine. The attack came on during sleep. A few hours later, he had another attack which seemed to be similar to the first, and two hours later another. Three months later, he had another attack at dinner, and was told that his left side had been rigid (probably incorrect). This attack lasted from twenty to thirty minutes. Additional attacks occurred six, ten and fifteen months later. Unilateral features were not noted in any of them except the one just quoted, but he has been told that his head usually turned to the right. There was no history of trauma.

Neurologic and Physical Examinations.—The results of the neurologic and physical examinations were negative. The Wassermann reaction of the blood was negative.

The ventricular system was dislocated to the right side, indicating a cerebral tumor on the left. The ventricular fluid was normal.

Operation.—On July 21, 1925, left craniotomy was performed. Five greatly dilated and somewhat tortuous veins stood out in strong relief on the surface of the brain. The rolandic and sylvian veins formed a relatively enormous continuous channel from the sylvian fossa to the superior longitudinal sinus. An almost equally large offshoot of the sylvian vein paralleled the rolandic vein and entered the longitudinal sinus, and two other branches of similar size passed downward from the sylvian vein to enter the transverse sinus. The latter veins, running closely together, formed en route a plexus over the temporal lobe. The red blood could be seen swirling in these veins with each pulse beat and mixing with the darker venous blood. The arteriovenous connection was deeper in the brain and could not be seen or palpated. The wound was closed without any attempt to treat the aneurysm.

Second Operation.—Two weeks later, the left common carotid artery was exposed under local anesthesia. After several transient compressions of the carotid

felt queer and that he could not swallow. It was observed that his right hand was drawn in the convulsion. A second convulsion occurred a year later; it resembled the first. A month later, the right side suddenly became completely paralyzed. Though he was unable to talk, he understood everything. There was some fever for three or four days and severe headache. A week later, the function began to return in the leg and arm, and in three weeks speech began to return. In three or four months, his speech was again normal, but there has since remained a slight residual weakness of the arm and leg. Further symptoms did not appear until two weeks before he came to the Johns Hopkins Hospital

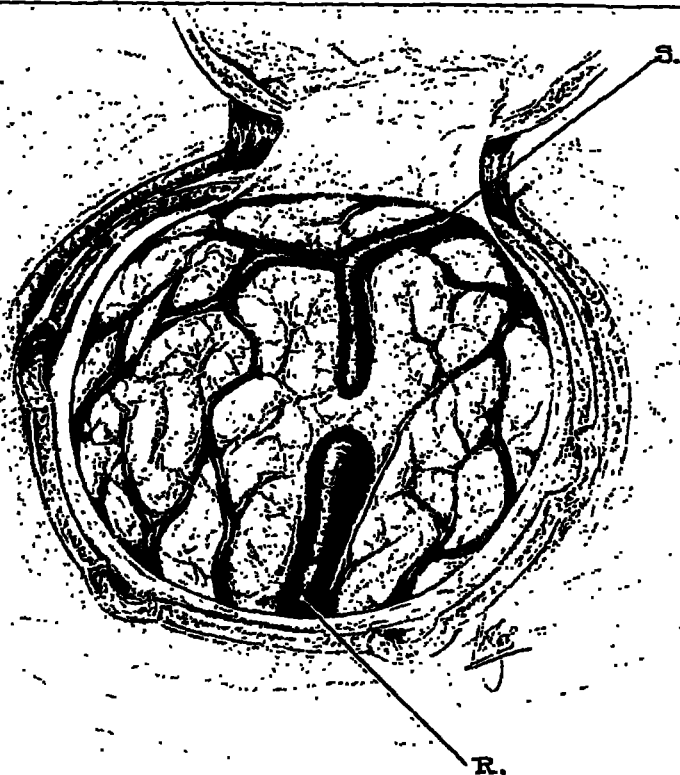


Fig. 22 (case 7).—The large rolandic vein can be seen coming directly out of the brain and has arisen from the vascular mass situated beneath. Arterial blood could be seen pumping into it. It will be noted that it has no connection with the group of veins below and which also comes out of the depth of the brain. The convolutions separate these two ends of the vein. The lower branch is continuous with the sylvian vein which is also large.

(October, 1926), when another attack began in the right hand. He had headaches only after attacks. There was no history of trauma.

Examination.—The neurologic examination showed the following positive symptoms: definite weakness of the facial muscles, the right hand, arm and leg; some atrophy of the right side; increased deep reflexes on the right; no ankle clonus, and a positive Babinski sign on the right.

The roentgenogram was negative. The Wassermann reaction of the blood was negative.

Pagan, of Washington, D. C., because of deforming veins of the scalp. Since early childhood (at least since she was 2 years of age), a lump had been present in the midline of the scalp and between the parietal eminences. It had always pulsated, but had been soft and painless. It had not given her any trouble, and had not grown in later years. Nine years before, when her first child was born, a lump, thought to be a big vein, appeared in the middle of the forehead. This swelling grew forward and became larger spasmodically; during each of seven pregnancies, it increased in size until it overhung the bridge of the nose and extended over to the inner canthus of each eye. Many other large tortuous veins



Fig. 24 (case 8).—Ventriculogram showing the small left anterior horn as compared with the normal on the right.

filled the scalp and became steadily larger until they began to encroach on the outer canthus of both eyes. The patient again became pregnant and was anxious about the vein increasing in size at the time of delivery. There had been no signs of intracranial pressure, though intermittent general headaches had been present for four or five years. On one occasion she had had an attack of numbness involving the right hand and lasting two weeks, but consciousness was not lost. There was no motor weakness during the attack, or at any other time. Noises in both ears had appeared recently and were somewhat annoying.

without subjective or objective noticeable change, the artery was ligated just below the junction of the internal and external carotid arteries. Manometric readings of the spinal fluid were made at the time of compressions of the internal carotid artery (lumbar puncture was performed at this time). With each temporary closure of the common carotid artery, the pressure of the spinal fluid fell from 240 to 215 mm. The pressure returned to its former level when the arterial compression was released. The blood pressure rose from 104 to 110 immediately after the ligation.

It should be noted that for several days before the ligation, the carotid artery was compressed on many occasions by pressure on the neck and without symptoms; the results indicated that the operative ligation would probably be safe.

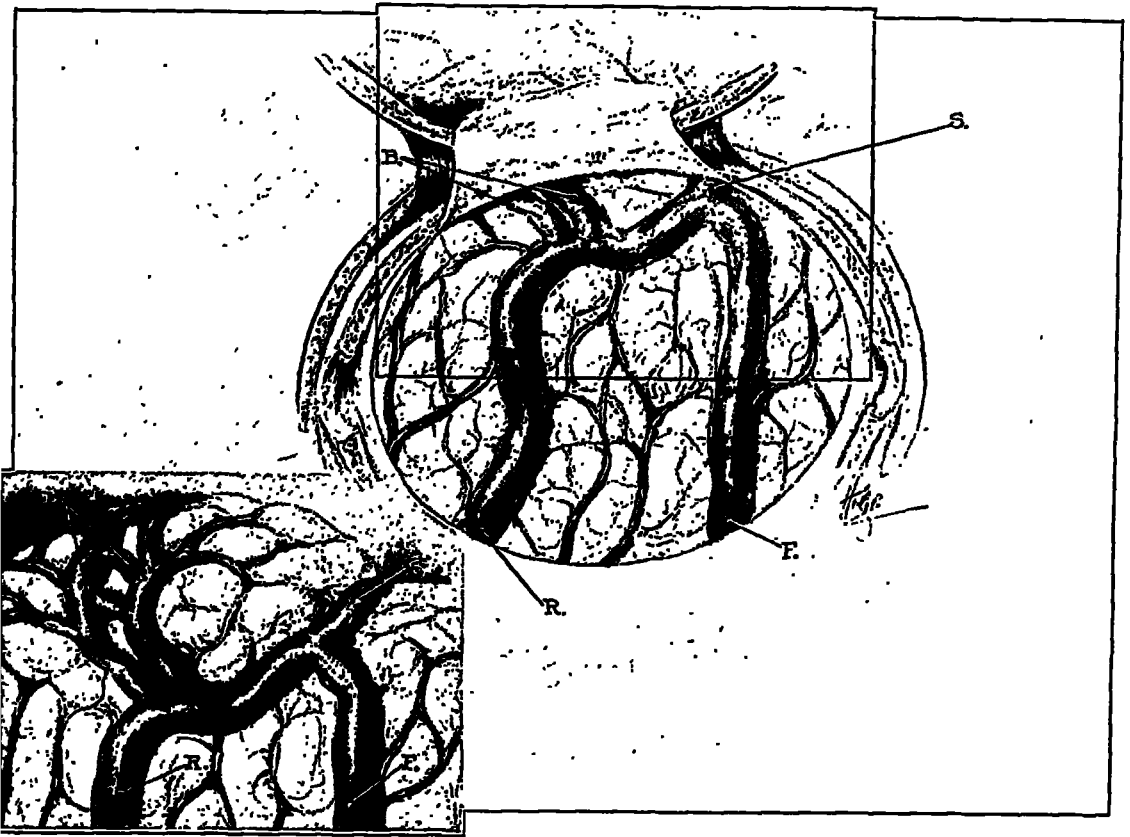


Fig. 23 (case 8).—Showing the distribution of the large distended veins on the surface of the brain and also the cluster of veins over the temporal lobe. Arterial blood could be seen pumping into these tremendous channels. As this aneurysm involved the most important part of the brain no attempt was made to treat the aneurysm directly. The left internal carotid artery was subsequently ligated. *R* indicates rolandic vein; *S*, sylvian vein; *F*, frontal vein; *B*, veins to lateral sinus.

The patient has remained free from both petit and grand mal attacks to date (two and a half years). There have been no untoward symptoms as a result of the closing of the common carotid artery.

Extracranial Arteriovenous Aneurysm—the Prototype of the Intracranial Lesion.—A well nourished, healthy woman, aged 29, was referred by Dr. A. E.

therefore, eliminated by the test. Palpation of the veins failed to disclose an arterial pulsation. A slight murmur could be heard over the veins when examination was made with a stethoscope. A thrill could be definitely made out over the large median vein and in other veins near the tumor. The greater the distance from the tumor, the less distinct the thrill became. The degree of pressure must



Fig. 26.—Arteriovenous aneurysm of the scalp which doubtless had intercranial extensions since the patient had localized sensory involvement of the right hand at one time. This lesion is a prototype of the intercranial aneurysm shown in figure 20. A localized mass posteriorly corresponds with the so-called angioma.

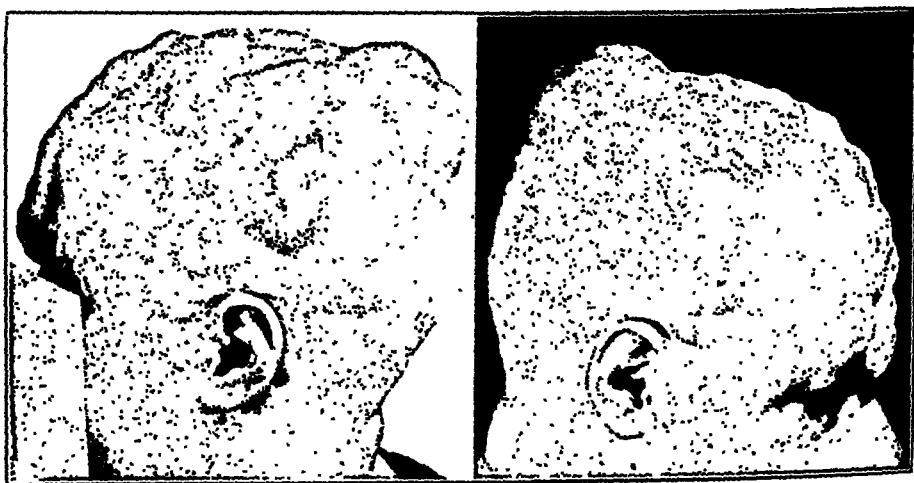


Fig. 27.—Same as patient in figure 26.

be just right to elicit the thrill. All of the veins were easily compressed. The tumor mass itself gave a strong expansible pulsation. The tumor was fairly soft and partly compressible, giving the impression of a mass of angle worms. When the mass was compressed firmly, it became painful and induced headaches. Compression could not be tolerated for more than a few minutes, nor could a number

Examination.—A pulsating tumor about as large as a lemon was palpable in the midline of the head between the parietal eminences. When the whole head was shaved, this mass was easily visible. From this tumor, as from the hub of a wheel, a number of enormous, tortuous veins coursed posteriorly, laterally and anteriorly (fig. 27). Pressure on the jugular veins promptly caused them to become tight and much fuller. Pressure on certain veins caused the distal portion to collapse, but the collapsed portion nearly always filled up slowly from collateral channels; when the collateral channels also were compressed, the distal part of

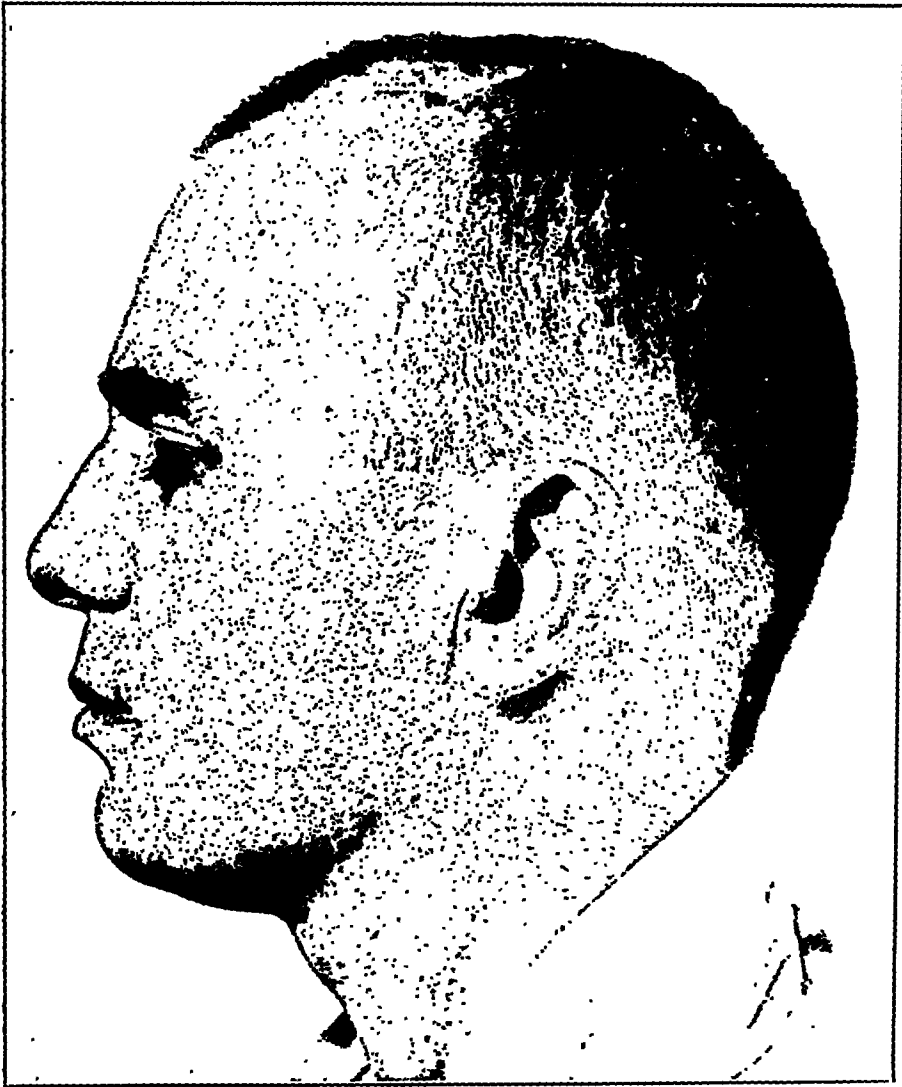


Fig. 25 (case 8).—Patient after ligation of the internal carotid artery in the neck.

the veins remained collapsed and did not fill (fig. 28). Particular reference is made to this point because of the large midline vein which extended to the nasion. When the collapsed venous space was palpated, it felt rough and one received the impression that there was a groove in the bone; until this test was made we wondered whether there might not be communication with the superior longitudinal sinus situated immediately beneath. The possibility of this communication was.

TABLE 1.—Analysis of Author's Eight

| Case, Age, Sex* | Location of Vascular Tumor | Duration of Symptoms | First Symptom | Principal Symptoms | General Pressure Signs and Symptoms | Focal Symptoms | Roentgen-Ray Observations | Eye-grounds |
|-----------------------|--|-------------------------|---|--|--|--|---|----------------|
| I 52 ♂ | Right temporal lobe | 6 yr. | Convulsion (general) | Convulsions (grand and petit mal); headache (1 week); sore- ness right tem- ple (1 week) | Headache (1 week) | Head turns to left in convul- sion; some subjective numb- ness in fingers of left hand | Negative | Normal |
| II 19 ♂ | Right parietal lobe | 4 yr. | Convulsion | Jacksonian convulsions often followed by weakness of left hand | None | Jacksonian convulsions beginning in left side of face | Negative | Normal |
| III 35 ♂ | Cerebellar left verte- bral artery | 2 yr. | Staggering gait | Staggering gait, diplopia, head- ache, dizziness, dysarthria; mental im- pairment. | Headache; choked disk; hydrocephalus | Staggering gait, Romberg, deafness | Negative | Choked disk |
| IV 47 ♂ | Fronto- parietal right | 6 yr. | Focal con- vulsions | Convulsions; motor loss on left side | None | Left hand, arm and leg involved in convulsion; motor weakness left arm | Extensive shadows in right fronto- parietal region | Normal |
| V 48 ♂ | Parieto- occipital right | 10 yr. | Convulsion | Convulsions; cerebral hemor- rhage, moody and forgetful | None, except during cere- bral hemor- rhage from which he recovered | Left side in- volved in attacks; left paresis, anes- thesia, and hemi- anopsia after cere- bral hemorrhage, later disappeared | Negative | Normal |
| VI 31 ♂ | Temporo- occipital | 15 yr. | Transient visual dis- turbances | Headache, con- vulsions, hemi- plegia, hemian- esthesia, hemi- anopsia, diplopia | Choked disk; headache | Hemiplegia, hemi- anesthesia, hemi- anopsia, focal convulsions (left side) | Large cir- cular hole in right occiput | Choked disk |
| VII 14 ♂ | Parietal | 7 yr. | Attack of weakness in right hand | Convulsions (Jacksonian); weakness right side of body; symptoms for cerebral hemor- rhage on one occasion | None | Weakness right side of face, right arm and leg; at- tacks beginning in right arm; motor aphasia and hemiplegia after cerebral hemorrhage | Linear calcified shadow | Normal |
| VIII 35 ♂ | Left parietal | 14 mo. | Convulsion | Convulsions | None | Head turns to right | Negative | Normal |

* In this table and the following tables, ♂ indicates male; ♀, female.

of veins be compressed at one time without causing pain and headache—doubtless for the same reason. Temporary occlusion of the veins caused the central tumor to become full and tight.

The roentgenogram showed large grooves of the middle meningeal artery on both sides; both grooves extended to the midline and appeared to end directly beneath the tumor of the scalp, otherwise the roentgenogram was negative.

The results of the neurologic examination were negative. The Wassermann reaction of the blood was negative.

A diagnosis of arteriovenous aneurysm of the scalp was made. The large channels of both middle meningeal arteries and the focal numbness of the hand made it seem probable that there was an intracranial extension of the aneurysm.

Operation.—The tumor itself was not removed, for intracranial extension was feared, because of the numbness of the hand which had been present for two



Fig. 28.—The collapse of the vein over the forehead when the arterial supply is cut off from the vascular mass. The venous channels then become greatly sunken.

weeks. The superficial temporal, internal maxillary and occipital arteries were ligated on both sides of the neck. On the left side, the external carotid artery was also ligated at its origin. After ligation of the arteries, the veins responsible for the tumor on the forehead were ligated. The veins responsible for this part of the swelling had previously been determined by compression with the fingers. The disfiguring part of the venous bed at once disappeared and has not returned. The redundant part of the skin disappeared and no sign of the old deformity remained. A few days after the operation, all of the veins in the scalp became hard and tender and were no longer compressible. Apparently they had thrombosed, and when the patient was seen six months later, all trace of them had disappeared. The central tumor mass had greatly diminished in size and no pulsation could be detected. The tinnitus had ceased. The patient had been well in every respect.

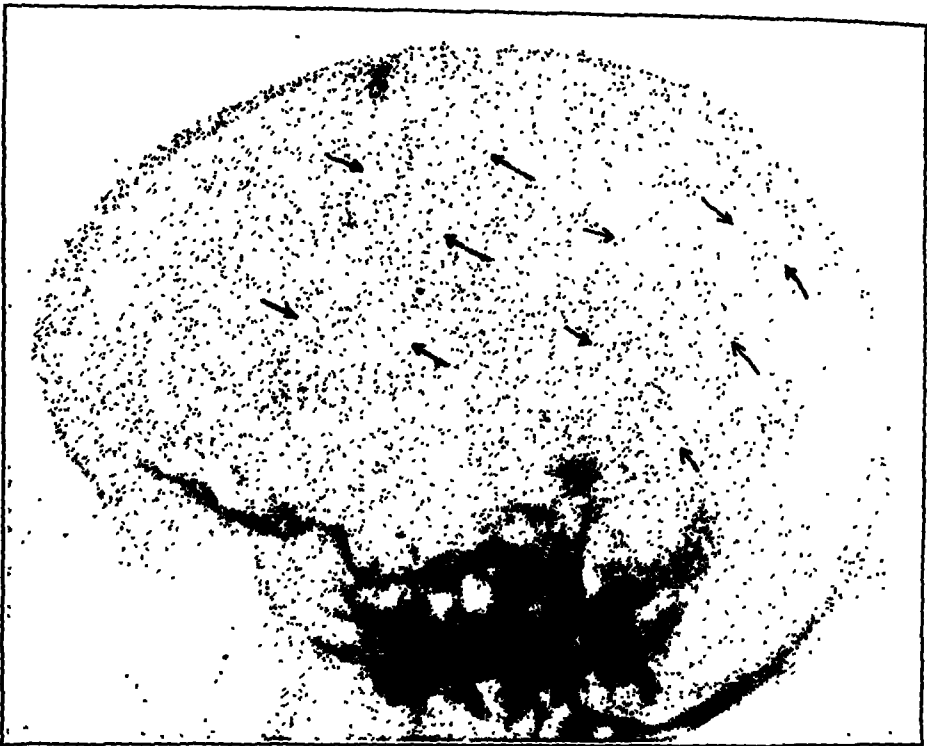


Fig. 29.—Greatly enlarged meningeal grooves, both right and left, directed toward the vascular bed of this aneurysm (interior set of arrows). The posterior set of arrows show the greatly enlarged venous channels in the skull providing exit for the blood leaving the vascular tumor, i. e., to the lateral sinuses.

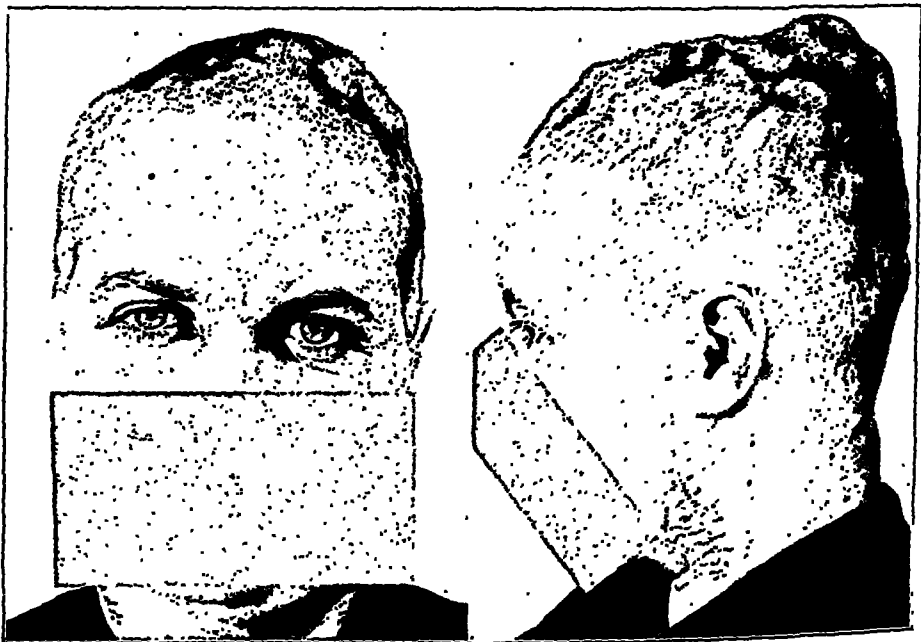


Fig. 30.—Result two weeks after the operation at which the occipital, posterior auricular, internal maxillary and superficial temporal arteries were ligated on both sides, and in which the venous channels were ligated at the two points indicated by the pressure of the fingers in figure 28. Several months after this photograph was taken all the veins had subsided and the pulsation in the arterial mass had ceased.

Cases of *Arteriovenous Aneurysms*

| Headache 1 week only | General Epilepsy | Focal Epilepsy Head turns to left | How Diagnosed Ventriculo- graphy and craniotomy | Diagnosis before Operation or Autopsy Tumor of the brain | Operations and Observations Anomalous branch of right middle cerebral artery supplied vascular mass; after its ligation, in a s s of venous vessels collapsed | Condi- tions at Necropsy Living | Remarks Patient has had but one attack since op- eration (3½ years); never had headache; general health excel- lent |
|----------------------------|---------------------|--|---|---|--|---|---|
| None | .. | .. begins in left face and arm | Craniotomy | Tumor of the brain | Mass of serpentine ves- sels with large emerg- ing veins; attempted extirpation; vessel burst between the liga- tures | | Patient died of hemor- rhage |
| | None | None | Neurologic signs of local- ization; crani- bellar explora- tion | Tumor of the brain | (1) Cerebellar explora- tion; (2) ligation left vertebral artery | Living | Patient's general pres- sure and neurologic signs and symptoms largely disappeared, but mental changes persisted |
| None | .. | .. left arm | Roentgeno- gram | Aneurysm of the brain | (1) Exploration of aneu- rysm; (2) internal carotid later ligated | Living | Attacks returned after a year's absence fol- lowing operation; the shadow in the roent- genogram was the im- portant diagnostic sign in this case |
| None | - | .. | Ventriculo- lography | Tumor or aneurysm (because of cerebral hemor- rhage) | Excision of vascular tumor | Shows arterial trunk from middle cerebral supplied tumor | Cerebral hemorrhage from the vascular mass |
| Severe | .. | + | By external arteriovenous vascular bed | Arterio- venous aneurysm | (1) Extracranial arterio- venous aneurysm (dis- sected out); (2) mass of angle worms in tempo- ro-occipital region; big veins (in cortex) with arterial pulsation | Living | Two separate arterio- venous aneurysms present, one in the scalp, the other in the brain |
| None | .. | + | Ventriculo- lography, history and exploration | Tumor or aneurysm | Big venous dilatation in which arterial blood could be seen | Living | Patient gave history of a cerebral hemorrhage, one year after first symptoms |
| None | + | Head turns to right | Ventriculo- lography | Tumor of the brain | (1) Large distended ro- landic and sylvian veins; arterial blood seen (through wall of vein) to be pumping into venous blood; venous plexus over temporal lobe; (2) internal carotid artery ligated | Living | Has had no attacks to date (2½ years) |

THE GROSS APPEARANCE OF ARTERIOVENOUS ANEURYSMS

The venous trunks draining the aneurysms (when located in the cerebral hemisphere) nearly always connect with the external venous circulation through the rolandic and sylvian veins, and when these form a continuous channel, as they usually but not always do, both show the maximum effect of the arteriovenous connection. This is evidenced by their dilatation throughout their course. The degree of involvement of the contiguous veins varies in individual cases; at times other nearby veins may be almost unaffected. In a single case, the venous outlet was through the internal venous system (Steinheil); one small vein of Galen and the great vein of Galen were dilated and tortuous throughout their course to the sinus rectus. In addition, a sacculated aneurysm with a long pedicle was present on the vein of Galen.

Because the external venous system carries the outflow of blood from most of the arteriovenous connections, the characteristic venous changes are on the surface of the brain. This makes it possible to detect these cases so easily at operation. And since the veins are free from all accessory coverings, it is also possible to see through their walls and detect the pulsing red, arterial blood against a background of black venous blood. This opportunity does not exist elsewhere in the body. So far as I am aware, attention has not been directed to this point—so essential to the diagnosis—heretofore.

In many of the cases of arteriovenous aneurysms located in the cerebral hemispheres, there are congenital abnormalities of the venous system on the exterior part of the hemisphere. In one case, the rolandic vein arose directly out of the brain substance, having its origin in the aneurysm. In two other cases, the rolandic vein did not exist as a well defined venous channel.

The degree of venous engorgement is dependent on the size of the arterial supply and on the size of the mass of vessels, or rather on the size of their lumina, forming the arteriovenous communication. A large angioma with many vessels takes some of the brunt of the arterial force off the venous channels of exit. A small angioma or a short connecting link throws all the arterial force directly into the veins. The smaller the artery and the smaller the lumen of the arteriovenous communication (i.e., the larger the number of vessels intervening between the artery and veins), the smaller will be the venous channels which drain the aneurysm. And conversely, the larger the artery and the larger the lumen of the arteriovenous connection (i.e., the smaller the mass of vessels between the artery and vein), the greater will be the effect on the veins emerging from the aneurysm. Many large veins, therefore, indicate a small angioma or a free end to end communication between an artery and vein. Smaller veins indicate a larger angioma and an arteriovenous

In retrospect, there is reason to believe that removal of the mass might have been safely performed without ligation of the branches of the external carotid. The result, however, would not have been different.

SEX AND AGE AND TIME OF APPEARANCE AND DURATION OF SYMPTOMS IN CASES OF ARTERIOVENOUS ANEURYSM OF THE BRAIN

In the literature, twelve of the cases of arteriovenous aneurysm of the brain reported occurred in men and eight in women. Curiously, the eight patients in the cases reported in this paper were men, but there seems to be no reason to lay emphasis on this point or to expect any differences due to sex.

The time of appearance of convulsions or the other more occasional symptoms is one of the most surprising features of this lesion. Being surely of congenital origin, it would be logical to expect symptoms soon after birth. Data on this point are available for eighteen of the thirty cases as follows: The first symptoms appeared in seven patients between the ages of 1 and 10; in three patients between 11 and 20; in three patients between 31 and 40; in five patients between 41 and 50; there was no record of first symptoms for patients between 21 and 30 years of age.

In 44 per cent of the patients, therefore, the first symptoms did not appear until after the age of 30 and in 30 per cent, symptoms began after the fortieth year. The latest time of appearance was at the age of 48.

The duration of symptoms ranged from a few hours to fifty years. In four of eighteen cases, symptoms had been present for more than twenty years.

LOCATION OF INTRACRANIAL ARTERIOVENOUS ANEURYSMS

The aneurysms are located in almost every part of the brain. Three are in the cerebellar region (Leunenschloss,²⁷ Znojensky,²⁸ Dandy). In one case (Znojensky) there were two separate and distinct aneurysms: one in the right cerebellar lobe, the other in the cerebral hemisphere. In two instances, there were arteriovenous aneurysms in the scalp, apparently independent of the intracranial lesion (Mühsam, pulsating exophthalmos; Dandy, occipital artery and mastoid vein).

An overwhelming proportion of the aneurysms are located in the paracentral region and have arterial connection with a branch of the middle cerebral artery. In two cases, the corpus callosal artery suggested the arterial connection (Deetz,²⁹ Steinheil³⁰).

section. The walls are at times thin, suggesting veins, and others alongside are thicker, suggesting arteries. The intima may be narrow, but frequently it is greatly thickened and at times irregularly so. Many vessels are entirely occluded by thrombus formation. The elastic fibers are shown in special stains to be present in the intima of many vessels but not in others. Rarely is the elastic tissue a well defined layer; usually a strand is present here and there. The media is usually poorly developed, with much hyaline degeneration or calcification. These changes, while doubtless varying considerably in detail, are essentially similar in all microscopic reports in the literature. They indicate abnormal, poorly developed vessels with debilitated walls, which render the person the victim of vascular rupture long before the allotted time for normal vessels. The extensive thrombosis has been commented on by several authors (Emanuel,³² Therman,³³ Leunenschloss,²⁷ Astwazturoff,⁹ Kaiserling³⁰). It is doubtless one of the important reasons for the progression of the lesion in the later years of life. Each thrombosed vessel throws an additional strain on the venous system and on the angiomatous mass. Doubtless it is this added strain which is also responsible for many of the hemorrhages. The intercommunication of the vessels within the vascular nest has been described. I have been unable to learn whether or not this was true in case 2 which came to necropsy, for the mass was mutilated during its removal. Simmonds¹⁶ reported evidence of canalization of thrombi.

SIGNS AND SYMPTOMS OF ARTERIOVENOUS ANEURYSM OF THE BRAIN

(a) *Convulsions*.—With four exceptions, the first symptom in this group of cases was a convulsion, and most of these (all but two) were of the jacksonian type. The starting point of the seizures, i.e., the aura, when present, varied with the exact point at which the motor or sensory tracts were involved. It is, of course, not necessary that the attacks show the jacksonian march; at times even the focal or unilateral character of the attacks may be none too clear, though probably in all cases there will at least be turning of the head to the opposite side. Jacksonian attacks are present only when there is a direct infringement on the motor tracts. Those aneurysms at a distance from the motor tracts will give less conspicuous unilateral signs in the attack, and usually no aura. In two of the cases reported here, there were no warning signs (aura). In both of the cases without jacksonian convulsions the head

32. Emanuel, C.: Ein Fall von Angioma arteriale racemosum des Gehirns, Deutsche Ztschr. f. Nervenhe. 14:288, 1898.

33. Therman, E.: Ein Fall von Angioma racemosum cerebri, Arch. a. d. path. Inst. d. Univ. Helsingfors 3:67, 1910.

communication which is relatively well compensated, i. e., nearer the function of the capillary system. Doubtless there are many smaller arteriovenous aneurysms with a small arterial inlet and relatively small veins of exit which could not be established as abnormal. A thrill could not be felt in these, nor could arterial blood be seen pumping into them. There have been several cases at the Johns Hopkins Hospital which showed definite vascular abnormalities and which were thought to be arteriovenous aneurysms, but these have been excluded from all consideration because the absolute evidence was lacking.

Kaiserling's³⁰ case and case 1 in my series are excellent examples of excessively large and tortuous veins which result when no barrier is interposed between an artery and a vein. In Kaiserling's case, a tortuous elongated artery could be seen emptying directly into a huge venous chamber. In case 1, a short anomalous branch of the middle cerebral artery, and with normally thick arterial coats, abruptly passed into a vein. The transition between the thick arterial and the thin venous coats was clearly seen during the inspection of the vessel. Reid's case³¹ of an arteriovenous aneurysm between the subclavian artery and veins in the neck seems in every way an exact duplicate of this case in the brain.

A mass of vessels forming the connection between the artery and veins, i. e., the so-called angioma, when such is present, is usually in the depths of the brain, but this is not necessarily true. In case 6, the mass was external, at least in large part. The gross character of the mass of entwined vessels is also variable: some look exactly like arteries, some like veins, and some like a combination of arteries and veins.

The arteries supplying the mass of vessels have always been larger than normal; some have been very tortuous (Deetz,³² Simmonds,³³ Kaiserling³⁰). In the only case of my series in which the artery was observed, the middle cerebral artery was enlarged all the way to the internal carotid artery. It was not tortuous, nor was its enlargement excessive—perhaps from one-third to one-half larger than the corresponding vessel of the opposite side (fig. 16). The arterial change, while always definite, is never comparable to that of the veins, which is really the characteristic part of the picture of arteriovenous aneurysm.

HISTOLOGIC APPEARANCE OF THE VESSELS IN SO-CALLED ANGIOMA

Steinheil¹⁰ and was present in two of the cases in my series, one permanently, the other only transiently after a cerebral hemorrhage. Simmonds¹⁶ reported blindness in one eye and loss of smell and taste. The reflexes on the contralateral side of the body are, of course, always increased when a motor weakness exists; often ankle clonus and usually a positive Babinski are also present under the same conditions. Deist's patient had a positive Babinski sign, even though motor weakness was not apparent.

Mental changes have been uncommon. Steinheil's patient became demented. One of the patients in my series became moody and was forgetful after recovery from a cerebral hemorrhage.

(d) *Cardiac Changes.*—Hypertrophy of the heart has been shown to occur in dogs after the production of arteriovenous fistulas (Reid,⁵ Holman⁷). Some of the cases reported by Reid and Holman also showed cardiac hypertrophy and even decompensation, for which they assumed the arteriovenous fistula to be responsible. Since enlargement and tortuosity of the arteries always follow a fistula, it is easy to believe that the heart too must suffer. Holman produced measurements to indicate that the size of the heart was actually reduced after the cure of an arteriovenous fistula. Emanuel,³² Isenschmid²⁶ and Laves³⁵ found cardiac enlargement in their cases and attributed it to the effects of the aneurysm. The heart was not found to be enlarged, or its function disturbed in any of the cases reported here.

(e) *Signs and Symptoms of General Pressure.*—In only seven of the thirty cases was there a history of headaches (Mühsam,¹² Simmonds,¹⁶ Eiselsberg,¹³ Emanuel,³² Dandy, [three]). This is noteworthy when the great size of the lesion is considered. The space adjustment, however, has occurred in early life and only gradual changes usually occur thereafter, excluding, of course, the always overhanging possibility of a sudden hemorrhage. In one of my patients, a man of 52, a headache had been present for only a week prior to the patient's admission to the hospital; his headache was sharply localized to the right frontal region owing to the fact that the vascular bed was in contact with the meninges. The headaches in other cases have been generalized. The patient of Campbell and Ballance and three of the patients in my series had severe headaches after each attack. Emanuel's patient was excused from military duty because of severe headaches which persisted throughout youth and finally disappeared; his head was also large.

Few examinations of the eyegrounds are reported in the assembled cases. A papilledema is reported only by Mühsam. The eyegrounds were carefully examined in all of our cases. In six, there was no change; in two, a well advanced choked disk. The pressure in one of these was due to an obstructive hydrocephalus; the cerebellar lesion had

turned away from the side of the aneurysm and eventually in each other unilateral features presented.

In a number of instances, consciousness was not lost in the attacks even when the seizure involved an entire side of the body. (Deist,³⁴ Laves,³⁵ Steinheil,³⁶ Dandy). Later, as the attacks became more severe, the other side of the body also became involved and consciousness was lost.

Indeed convulsions need not occur even though the motor or sensory areas are involved. Only two cases in which the cerebral hemispheres were involved failed to cause epilepsy (Simmonds,¹⁶ Struppler¹⁵). Two cases of cerebellar arteriovenous aneurysms involving the cerebellum failed to produce convulsions (Leumenschloss,²⁷ Dandy), but tumors in the cerebellum or the posterior cranial fossa rarely cause epilepsy,

(b) *Motor and Sensory Disturbances.*—Another important and frequent sequel of the convulsions is a transient sensory or motor paralysis. This occurred in nearly all of the cases which have been reported. Sensory or motor weakness following a convulsion is strong evidence in favor of a tumor of some kind. When the same motor involvement occurs repeatedly with such precision of attack and over a period of so many months or years and with little or no permanent progression, an arteriovenous aneurysm would appear to be the most probable lesion. The paralysis often does increase slowly in these cases, for the volume of the vascular network must slowly increase, especially in later life. It will be remembered that the degenerative and proliferative changes (calcification and thrombosis) which occur prematurely in the angiomatic mass must from time to time demand readjustments and always the volume of the network of vessels must expand in this process, thereby causing increased paralysis.

Sudden hemiplegia or hemianesthesia are the results of hemorrhage, which is so prone to occur at any age, but particularly during advancing years. Usually the paralysis disappears, in part or whole, the amount of recovery depending on the proximity of the aneurysm to the motor or sensory tracts.

(c) *Other Focal Signs and Symptoms.*—Other focal manifestations are at times present. Transient attacks of aphasia occurred in the cases of Ranzel³⁶ and Sterzing.³⁷ Homonymous hemianopsia was noted by

34. Deist, H.: Ein Fall von Angioma racemosum der linken Lobus paracentralis in seiner klinischen und versicherungsrechtlichen Bedeutung, Ztschr. f. d. ges. Neurol. u. Psychiat. 79:412, 1922.

35. Laves, W.: Ein Fall von Angioma arteriale racemosum des Gehirns, Jahrb. f. Psychiat. u. Neurol. 44:55, 1925.

36. Ranzel, F.: Zur Kasuistik kombinierter Hirnaffektionen; ein Fall von Rankenangiom des Gehirns mit tuberculous Meningitis, Wien. klin. Wchnschr. 22:1214, 1909.

37. Sterzing, P.: Ein Fall von Angioma arterial racemosum im Gehirn, Centralbl. f. allg. Pathol. u. path. Anat. 19:278, 1908.

Roentgenologic Evidence.—The results of the roentgen-ray examination were of great importance in two cases. In one case, a probable diagnosis of an intracranial aneurysm was made principally on the basis of the roentgen-ray examination. A series of calcified shadows covered an area roughly circular and about 5 cm. in diameter; all were beneath the surface of the brain. While most of the shadows had no unusual shape, circular or spiral, the shape of three of this group suggested calcium deposition in the walls of the blood vessels. In fact, such shadows could hardly be produced in any other lesion (excepting of course calcified blood vessels in tumors).

In a second case, a linear shadow, 1.5 cm. long, could be seen along the anterior horn of the lateral ventricle. This shadow, however, was visible only after the ventricle had been filled with air, which afforded an excellent contrast medium for the background. In a third case, a circular hole about 1 cm. in diameter, located alongside the mastoid, was clearly shown in the roentgen ray. The importance of this roentgenographic evidence, however, was minimized because it was readily palpable, being large enough to admit the tip of the index finger.

The large middle meningeal grooves (bilateral) commented on in the history of the extracranial arteriovenous aneurysm cannot be used as positive evidence because a cranial exploration was not made. As almost all of the intracranial aneurysms are located within the brain, there is little possibility of any vascular burden being referred to the middle meningeal arteries, and therefore the arterial vascular changes which are usually sought from this source in roentgenograms of the skull will be lacking. The positive roentgen-ray observations in cases of arteriovenous aneurysms of the brain will be largely confined to the calcified deposits in the abnormal vessels of the brain, or perhaps to localized areas of erosion. It is noteworthy that in two of the cases reported here, there was a localized erosion of the inner table of the skull, but the roentgenograms failed to disclose it.

VENTRICULOGRAPHY

The use of the air contrast medium in the cerebral ventricles is always important when the existence or even the character of an intracranial lesion is in doubt. Even though arteriovenous aneurysms only occasionally produce signs and symptoms of intracranial pressure, the lesion is one which occupies intracranial space, and therefore will usually give the positive evidence of a deformed ventricular system. Mention need not again be made of the calcified deposit which could be observed only with an air background, but such a condition is of less importance than the deformation of the ventricular system.

In two of the cases in my series in which the unilateral character of the attack was rather uncertain, the ventriculogram showed the entire

blocked the aqueduct of Sylvius. In the other case, a choked disk had been present for more than ten years. After a subtemporal decompression, the decompression was at times full and tight, again soft and even sunken. The great variations in pressure may account for the preservation of vision even with such a long-standing swelling of the eyegrounds.

Diplopia as a sign of pressure was reported only twice (Mühsam, Dandy).

(f) *Cerebral Hemorrhage*.—The premature degenerative vascular changes which have been commented on explain the frequency of cerebral hemorrhage in this group of cases. It is a fairly safe, but not absolute, rule that when a cerebral hemorrhage occurs during youth or middle age, i. e., before the time when vascular accidents are to be expected, there must be an underlying tumor or aneurysm, either of which will contribute defective vessels. In the twenty-two cases collected from the literature, nine patients, or 41 per cent, died of cerebral hemorrhage (Drysdale,³⁸ Kaiserling,³⁹ Borchardt,³⁹ Ranzel,³⁹ Simmonds,⁴⁰ Sternberg,⁴⁰ Sterzing,⁴¹ Wichern⁴¹ and Leunenschloss²⁷). Only two of the eight patients whose cases are reported herewith had a cerebral hemorrhage, one known and the other presumed from the history, but both patients recovered. The probability of death from cerebral hemorrhage from these lesions is also increased because in many instances the nest of vessels frequently projects into the lateral ventricle. A hemorrhage of smaller size may develop in the tumor or the contiguous brain tissue and may not induce coma, as in one of the eight cases; the hemorrhage seemed certain because of the sudden complete hemiplegia with slow recovery. Sterzing's case is a remarkable example of the capricious character of the defective vessels in the vascular network. His patient, who died of cerebral hemorrhage at the age of 32, had suddenly developed hemiplegia with disturbance of speech (presumably due to a cerebral hemorrhage) twenty-two years earlier when 10 years old. After a slow return of function, there had been no motor change until a year and a half before death, when the same side again became paralyzed; curiously, jacksonian convulsions did not develop until after this late attack of paralysis. Childbirth was an inciting cause of the cerebral hemorrhage in Borchardt's case.

38. Drysdale, J. H.: Report of Case, Pathological Society of London, *Lancet*, 1904, p. 96.

39. Borchardt, M.: Die chirurgische Bedeutung der Gehirnaneurysmen, *Beitr. z. klin. Chir.* 133:429, 1925.

40. Sternberg, C.: Demonstration eines Falles von Angioma arteriale racemosum des Gihirns, *Verhandl. d. deutsch. path. Gesellsch.* 7-9:308, 1905.

41. Wichern, H.: Klinische Beiträge zur Kenntnis der Hirnaneurysmen, *Deutsche. Ztschr. f. Nervenhe.* 44:220, 1912.

Roentgenologic Evidence.—The results of the roentgen-ray examination were of great importance in two cases. In one case, a probable diagnosis of an intracranial aneurysm was made principally on the basis of the roentgen-ray examination. A series of calcified shadows covered an area roughly circular and about 5 cm. in diameter; all were beneath the surface of the brain. While most of the shadows had no unusual shape, circular or spiral, the shape of three of this group suggested calcium deposition in the walls of the blood vessels. In fact, such shadows could hardly be produced in any other lesion (excepting of course calcified blood vessels in tumors).

In a second case, a linear shadow, 1.5 cm. long, could be seen along the anterior horn of the lateral ventricle. This shadow, however, was visible only after the ventricle had been filled with air, which afforded an excellent contrast medium for the background. In a third case, a circular hole about 1 cm. in diameter, located alongside the mastoid, was clearly shown in the roentgen ray. The importance of this roentgenographic evidence, however, was minimized because it was readily palpable, being large enough to admit the tip of the index finger.

The large middle meningeal grooves (bilateral) commented on in the history of the extracranial arteriovenous aneurysm cannot be used as positive evidence because a cranial exploration was not made. As almost all of the intracranial aneurysms are located within the brain, there is little possibility of any vascular burden being referred to the middle meningeal arteries, and therefore the arterial vascular changes which are usually sought from this source in roentgenograms of the skull will be lacking. The positive roentgen-ray observations in cases of arteriovenous aneurysms of the brain will be largely confined to the calcified deposits in the abnormal vessels of the brain, or perhaps to localized areas of erosion. It is noteworthy that in two of the cases reported here, there was a localized erosion of the inner table of the skull, but the roentgenograms failed to disclose it.

VENTRICULOGRAPHY

The use of the air contrast medium in the cerebral ventricles is always important when the existence or even the character of an intracranial lesion is in doubt. Even though arteriovenous aneurysms only occasionally produce signs and symptoms of intracranial pressure, the lesion is one which occupies intracranial space, and therefore will usually give the positive evidence of a deformed ventricular system. Mention need not again be made of the calcified deposit which could be observed only with an air background, but such a condition is of less importance than the deformation of the ventricular system.

In two of the cases in my series in which the unilateral character of the attack was rather uncertain, the ventriculogram showed the entire

those described in the typical cases, the diagnosis of arteriovenous aneurysm should at least always be strongly suspected.

Moreover, given sharply defined jacksonian convulsions, appearing in youth and continuing into adult life, with a gradually progressive

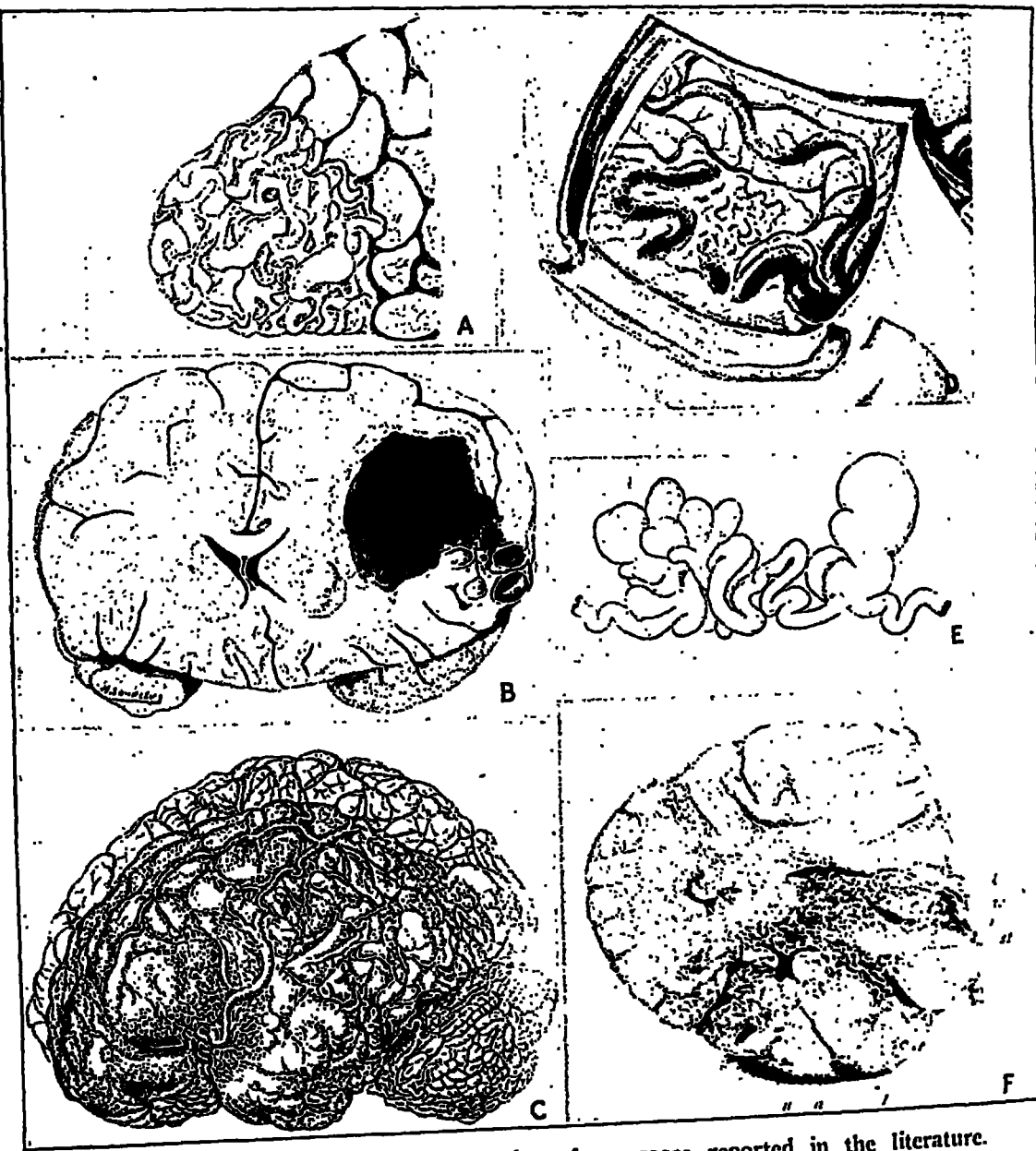


Fig. 31.—Group of specimens taken from cases reported in the literature. They show the variations which arteriovenous aneurysms may take in the brain. *A* indicates Simmond's case; *B*, Borchardt's case; *C*, Kalischer's case; *D*, Krause's case; *E*, Simmond's second case (the mass was dissected); *F*, Emanuel's case.

paralysis and then a superimposed cerebral hemorrhage such as afflicted so many of these patients, one could almost venture an absolute diagnosis of an arteriovenous aneurysm.

ventricular system to be dislocated to the opposite side. The roentgenographic changes do not, of course, make the diagnosis of an arteriovenous aneurysm; they only denote a space-occupying lesion. In another case, the ventriculogram indicated a large defect communicating with a lateral ventricle. Since the patient had previously had a history of cerebral hemorrhage, the ventricular hernia was assumed to be due to the localized hemorrhage which occurred on that occasion. But this cranial defect did not indicate the location of the aneurysm or tumor which had caused the hemorrhage.

Ventriculography yields much invaluable information in cases of epilepsy. It at once separates those lesions which are space-occupying. It will also demonstrate those lesions which are due to loss of brain tissue; also many of the congenital cerebral deformations. Even in cases of well defined focal or jacksonian epilepsy, ventriculography often yields most important information prior to a cranial exploration, for many lesions are below the cortex and would escape detection by inspection or palpation of the brain were the ventriculographic evidence not known at the time.

THE DIAGNOSIS OF ARTERIOVENOUS ANEURYSM OF THE BRAIN

The signs and symptoms of arteriovenous aneurysms show striking uniformity when taken as a whole. The outstanding complaints are: (1) jacksonian convulsions usually followed by (2) a transient motor or sensory disturbance, and (3) a gradually progressive and permanent motor or sensory paralysis coming on over a period of years and not directly depending on convulsions. When to these are added the long time element, the data are sufficiently characteristic at least to suggest the diagnosis of an arteriovenous aneurysm above other lesions affecting the brain. The transient paralysis following a convulsion and particularly the gradual permanent paralysis (not related to convulsions) makes a tumor formation of some kind an almost certain diagnosis. The accurately repeated jacksonian convulsions, involving such a sharply restricted part of the rolandic area and particularly when covering a period of so many years, should make a true neoplasm very unlikely. When the convulsions begin in early life and extend into the adult life, a neoplasm can almost be excluded. But when the epilepsy begins in later life and the time interval is still short, slowly growing tumors such as the meningiomas are important lesions to be differentiated; likewise they may show pressure symptoms late. Venous angiomas must always enter into consideration. They too will cause transient motor and sensory losses after the jacksonian seizures, but the permanent motor and sensory changes are far less possible, and when they do occur they are less progressive than in the arteriovenous variety. With symptoms, such as

Not infrequently a well defined extracranial arteriovenous aneurysm is demonstrable in patients who also have the intracranial signs and symptoms described for cerebral arteriovenous aneurysms. With such symptoms, an intracranial lesion of the same type is to be expected. An intracranial arteriovenous aneurysm was diagnosed in one of the cases reported here by this method of reasoning (case 6).

THE TREATMENT FOR ARTERIOVENOUS ANEURYSMS OF THE BRAIN

Occasionally spontaneous recovery in cases of arteriovenous aneurysm has been reported, but there is little real hope for such a successful outcome either in the brain or elsewhere in the body. The only way to cure an arteriovenous aneurysm is to ligate the entering artery or to excise the vascular tumor. But the radical attempt at cure is attended by such supreme difficulties and is so exceedingly dangerous as to be contraindicated except in certain selected cases. It has never seemed fair to make this attempt except on the insistent demand of the patient who fully understood all phases of the situation. Moreover, there are ways of helping the condition with little if any risk, and this in many cases at least seemed more to be recommended than the attempted extirpation of the vascular mass.

As in most cerebral lesions, however, each case should be considered a law unto itself. There are large aneurysms and small ones; those which are mostly arterial, others mainly venous; some are superficial, others deep; some are in highly important areas of the brain, others in portions largely silent. All of these factors, and finally the patient's wishes in the matter, must be weighed. An aneurysm in the left cerebral hemisphere in a right-handed person is surely *noli me tangere* under all conditions. Any attempted cure, even if successful, would almost surely result in disturbances of speech or motor power, or of both. Aneurysms of the corpus callosal arteries do not offer any greater surgical possibilities.

There is more reason to attempt to cure a patient who has arteriovenous aneurysms in the right cerebral hemisphere. In most of these cases, the arterial connections with the lesions are provided by branches of the middle cerebral artery. Should the aneurysm be postrolandic, the arterial connection can be ligated without injury to the motor function. In one case, we were able to do this without great difficulty. After ligating the arteries supplying the angioma, excision of the vascular bed was easy and relatively bloodless. In another case, in which the anterior pole of the right temporal lobe was covered with great tortuous and distended veins, the anomalous vessel was located and ligated with a silk ligature. It arose from the middle meningeal artery just beyond its origin from the internal carotid; following this the mass of distended

In those cases with the less well defined jacksonian convulsions developing in adult life and without a slow paralysis, one would have little reason to suspect an arteriovenous aneurysm; rather the diagnosis of a cerebral tumor would be considered most probable.

The roentgen-ray evidence, as in one of the cases which I have reported, may, unaided be sufficient for diagnosis. The presence of cal-

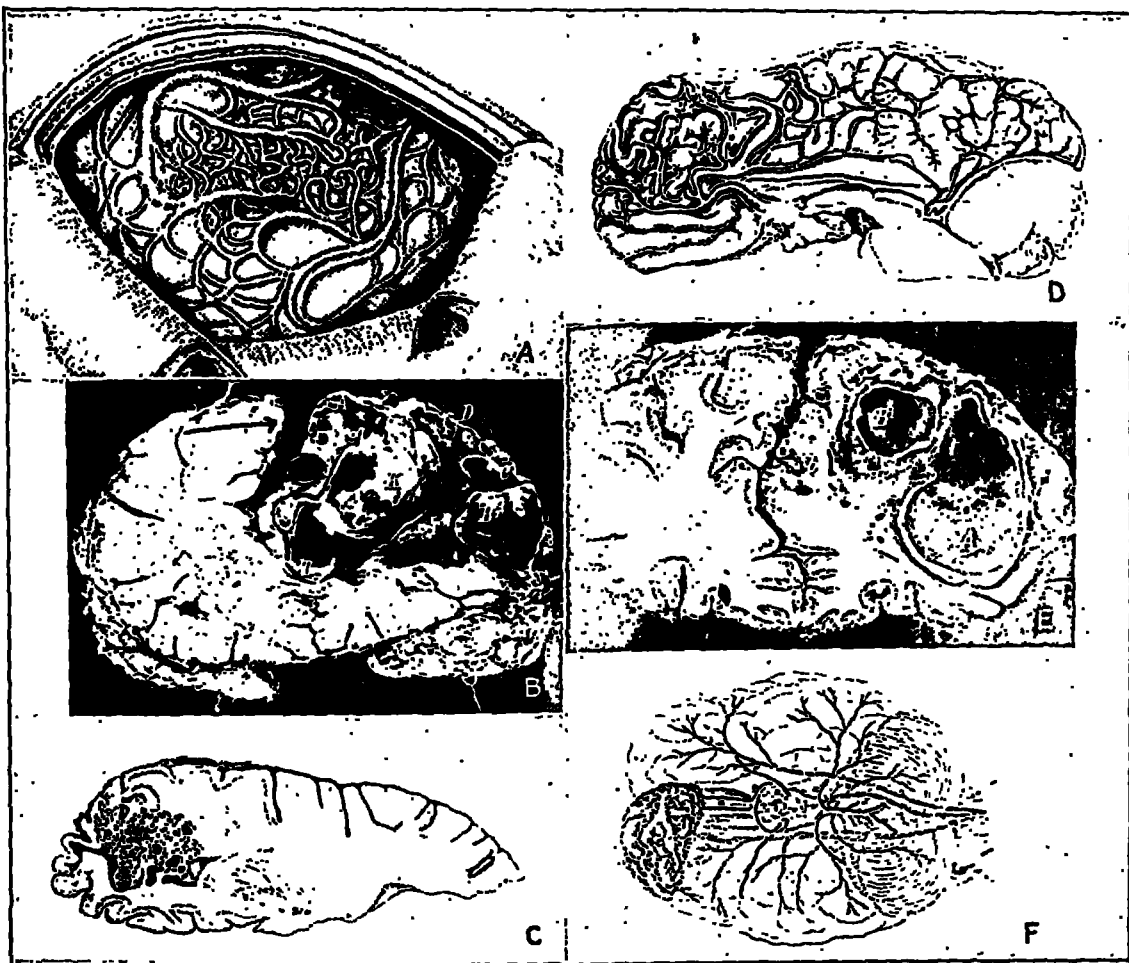


Fig. 32.—Group of specimens from the literature. *A* indicates Campbell and Ballance's case; *B*, Kaiserling's case. The arrow at the top of the brain is directed to the arterial venous connection which Kaiserling has marked *A*; the extensive thrombosis formation is marked *K*. *C* indicates Deetz's case showing the intracranial extension of the aneurysm; *D*, Deetz's case, in which the aneurysm arose from the corpus callosal artery; *E*, Kaiserling's case. This section is anterior to the one in *B*. *F* is taken from Steinheil's case in which the outlet of the aneurysm was into the vein of Galen.

cified shadows in circles or whorls, is, I believe, almost pathognomonic of vascular degeneration. When taken in conjunction with the clinical data, the diagnosis should be unequivocal.

TABLE 2.—Analysis of the Cases of Arteriovenous

| Author | Date, Sex, Age | Location | Duration Symptoms | First Symptom | Principal Symptoms | Sign or Symptom of General Pressure | Focal Symptoms | Eye- grounds |
|--|----------------------|---|----------------------|---|--|--|---|--|
| Bergmann ⁴² | | Fossa of Sylvius and paracentral fossa | .. | | | | | |
| Borchardt ²⁰ | 1925 ♀ 27 | Paracentral | .. | | Convulsions; paralysis | | | |
| Campbell and Ballance ¹⁴ | 1922 | Paracentral | .. | Weakness of arm and leg; and fits | Mild degree hemiplegia and anesthesia; convulsions | None | Hemiplegia and hemian- esthesia; increased reflexes; ankle clonus | |
| Deetz ²⁰ | 1902 ♀ 56 | Right side of corpus callo- sum | .. | Convulsion | Convulsions; partial hemi- plegia | None | Left hemi- plegia; Jack- sonian con- vulsions | |
| Deist ³⁴ | 1922 ♂ 56 | Paracentral (left) | 12 yr. | Convulsion | Convulsions | None | Jacksonian convulsions; Babinski + | Nega- tive |
| Drysdale ³⁸ | 1904 ♀ 26 | Prerolandic (right) | 11 yr. | Convulsion | Convulsions; weakness | | | |
| Eiselsberg ¹⁸ | 1913 ♂ 39 | Paracentral | .. | Convulsion | Convulsions; headaches | Headaches | Jacksonian convulsions | |
| Emanuel ³² | 1898 ♂ 36 | Paracentral | 30 yr. | Headaches when a boy | Convulsions | Headache; large head | Jacksonian convulsions | |
| Kaiserling ³⁰ | 1913 ♂ 26 | Most of hemi- sphere | .. | | | | | |
| Kallischer ¹¹ | 1897 ♂ 7 | Sylvian fossa and frontal lobe | 1 yr. | Convulsion | Convulsions; hemiplegia grad- ually became complete | None | Convulsions and hemi- plegia | Nega- tive |
| Krause ⁸ | 1908 ♂ 46 | Paracentral | .. | | | | | |
| Laves ³⁵ | 1925 ♀ 53 | Paracentral and post- rolandic | 12 yr. | | | | | |
| Mühsam ¹² | 1924 ♀ 25 | Occipital region | .. | | Diplopia; headache | Diplopia; headache | | Large tortuous vessels; slight choking |
| Ranzel ³⁶ | 1909 ♂ 36 | Left occipi- tal lobe | 2 yr. | Convulsion | Convulsions; some motor and speech disturbance | None | Jacksonian convulsion*, hemiplegia, aphasia | |

venous trunks collapsed. This patient has remained well for three and one-half years; he has had only one convulsion (a year ago), whereas before the fistula was closed, convulsions occurred every month. There is no assurance of a permanent cure of epilepsy even after the cure of an aneurysm. The cerebral defect will always remain at the site of the old lesion and any lesion of the cerebral hemisphere will always remain a potential source of convulsions. However, the convulsions will be far less and more easily controlled with an inactive lesion than with one which is active.

A third and only other attempt at radical cure by extirpation of the angioma was our first experience with a lesion of this type. Thinking at the time that it was a venous angioma, its extirpation after careful ligation of all the superficial veins seemed possible. The huge rolandic vein was doubly ligated and divided both above and below the great mass of cortical vessels and another vein was being sutured when suddenly the rolandic vein burst, not at the site of the sutures, but midway between them. It was then evident that the bleeding was arterial, and that with the venous outlets closed, the arterial pressure within the veins was greater than the wall of the vein would stand. The vein ruptured at the localized swelling shown in the drawing, i. e., at the weakest point and probably where the main force of the artery is projected. This accident demonstrated the danger of closing the veins while the arteries supplying the aneurysm are intact. When the second ligation was being placed on the big rolandic vein it was observed that considerable force was necessary to tighten the knot and occlude the vessel, and it could be done only step by step; the arterial pressure was responsible for this difficulty. Krause's case is interesting in this connection. He, too, ligated some veins on the surface, thinking the angioma to be venous and hoping to benefit the patient by reducing the number of veins. Fortunately nothing happened. He commented on the fact that the ligated veins "ballooned out like sausages." Bergmann's⁴² patient died from uncontrollable bleeding; assuming a localized bulge in the dura to be a cyst, a blind puncture into it was followed by terrific bleeding. Laves' patient also was lost on account of hemorrhage following an exploratory puncture of the brain. Once there is a tear in such a nest of vessels, their defective walls almost preclude all chance of controlling the bleeding. Each attempt at hemostasis is promptly followed by more bleeding.

In two of my cases in which the aneurysm was located in the rolandic and prerolandic areas, palliative treatment was tried, the internal carotid artery being ligated in the neck. In one case there have been no attacks.

42. Bergmann: Zur Kasuistik operativer Hirntumoren, *Arch. f. klin. Chir.* 65:935.

TABLE 2.—Analysis of the Cases of Arteriosclerosis

| Author | Date, Sex, Age | Location | Duration Symptoms | First Symptom | Principal Symptoms | Sign or Symptom of General Pressure | Focal Symptoms | Eye- grounds |
|-------------------------------|----------------------|-------------------------------|----------------------|--------------------|--|--|---|-----------------|
| Simmonds ¹⁴ | 1905 ♀ 18 | Right occipital lobe | 6 yr. | Headaches | Headaches, hemiplegia, loss of touch and smell; blindness right eye | Headache | Hemiplegia | |
| Astvazaturoff ⁵ . | 1911 ♀ 35 | Right fronto-parietal | .. | Convulsion | Convulsions; headache | Headache | Jacksonian convulsions | |
| Simmonds ⁹ | 1905 ♂ 55 | Right parietal | Since childhood | Convulsion | Convulsions | | | |
| Steinhell ¹⁰ | 1895 ♂ 49 | Right frontal | Since childhood | Convulsion | Convulsions; progressive paralysis and hemianopsia (left homonymous) | | Hemiplegia; hemianopsia (left homonymous); Jacksonian convulsions | Normal |
| Sternberg ¹⁰ | 1905 ♀ 25 | Temporal lobe | .. | | | | | |
| Sterzing ³⁷ | 1908 ♂ 32 | Corpus striatum | 22 yr. | Weakness right leg | Hemiplegia; convulsions; some motor aphasia | No | Hemiplegia; Jacksonian convulsions | |
| Struppler ¹³ | 1900 ♀ 48 | Paracentral | Few hours | Coma | None until coma | No | None | |
| Wiehern ⁴¹ | 1912 ♂ 32 | | .. | Hemiplegia | | No | Hemiplegia; Jacksonian convulsions | |
| Leunenschloss ²⁷ | 1914 ♂ 24 | Right cerebellar lobe | 15 yr. | Headache | Headache; hemiplegia; deafness; dizziness | Headache | Deafness | |
| Therman ²⁸ | 1910 | Parietal lobe | .. | | | | | |
| Znojensky ²⁸ | 1910 | Parietal lobe also cerebellum | .. | | | | | |

Aneurysm Collected from the Literature

| Head-ache | General Epilepsy | Focal Epilepsy | How Diagnosed | Diagnosis Before Operation or Autopsy | Operation and Observations | Conditions at Necropsy | Remarks |
|---------------|------------------|-------------------------|------------------------|---------------------------------------|--|---|---|
| .. | .. | .. | Operation and necropsy | Brain tumor | Large veins on surface of brain | Walnut sized knot of vessels beneath surface of brain, very tortuous | Puncture of dura blindly; terrific hemorrhage, uncontrollable, death; diagnosed cavernous angioma |
| .. | + right | .. | | | | Section shows aneurysm | Old specimen from Virchow Krankenhaus; patient died in childbirth of cerebral hemorrhage |
| After attacks | .. | + left toes | Operation | Tumor | Large veins on surface | Living | Hemiplegia and hemianesthesia were gradually progressive |
| .. | .. | + left-sided | Necropsy | | | Right corpus callosal artery large and tortuous; mass of vessels plunged into frontal lobe | Very extensive tumor covers mesial surface of hemisphere, fills frontal lobe and reaches anterior horn of ventricle and corpus striatum |
| None | .. | + right leg | Necropsy | | | Large veins on surface | |
| .. | .. | + arm and leg | Necropsy | | | Anterior cerebral artery very large; hemorrhage | Large veins on surface obscured brain; patient gradually became more and more deeply comatose following fit 10 days previously |
| + | .. | + right side | Operation | | Large veins on surface | | Very large veins on surface of brain; ligated; condition of patient unchanged |
| In youth only | .. | + arm | Necropsy | | | Large surface veins; mass of vessels in brain grown into ventricle and choroid plexus, also extended to pulmonary | Patient died in coma following attack; was excused from military duty because of headache; vessels are thrombosed and calcified; no mention of cerebral hemorrhage |
| .. | .. | + | Necropsy | | | Large surface veins | No history, except that patient died in coma following attack; this is a remarkable specimen, the veins and arteries being sharply defined; the communication is shown in the photograph; the venous channels are larger than in any other case; there is no network of vessels |
| None | .. | + right corner of mouth | Necropsy | | | Large veins on surface and mass of vessels in frontal lobe | No change in big arteries at base of brain; Virchow said it was an unusual case |
| .. | .. | + | Operation | | Ligated some veins, says they then distended like sausages | Large surface veins; smaller vessels of the tumor just reach the surface | Typical surface appearance of lesion shown in painting |
| .. | .. | + left hand | Operation and autopsy | | Large veins on surface; no thrill or pulsation | Cluster of entwined vessels below surface | No loss of consciousness in earlier attacks; at operation brain was punctured, severe bleeding which was uncontrollable; branch of middle cerebral artery (containing small sacculated aneurysm) enters vascular tumor which protrudes into ventricle; hypertrophy of heart |
| + | .. | .. | Necropsy | | | | A pulsating tumor nearinion connects with veins of brain and longitudinal sinus; also pulsating exophthalmos; very large veins in dura and in the brain seen on its surface |
| .. | .. | + right arm | Necropsy | | | Small knot of vessels in left occipital lobe | Patient died of hemorrhage in an attack |

either petit or grand mal, since the operation (two and one-half years). The other patient, roentgenograms of whom showed the extensive calcification, was free from attacks for a year, after which they gradually recurred with practically the same intensity and frequency as before operation. The latter patient being 47 years old, the carotid was at first only partially ligated with a band of rubber tissue. Three weeks later, it was found to be totally occluded by a thrombus.

A subtemporal decompression and excision of the extracranial aneurysm (of the scalp) were performed in another patient who was losing vision because of a long-standing papilledema. His headache was relieved, but his condition otherwise was unchanged.

The cerebellar arteriovenous aneurysm had caused hydrocephalus. This was relieved by the bilateral cerebellar decompression which, as a routine, remains after a cerebellar exploration. The decompression remained full and tight until it was later relieved by ligation of the left vertebral artery in the neck. At operation, the intracranial portion of this artery was found to be several times its natural size, and this led to the belief that it supplied the arterial connection to the aneurysm. When exposed between the atlas and occipital bone, this great tortuous artery was just as large as the intracranial portion. Following its ligation, the bulging decompression subsided and has remained in this condition. Although his neurologic symptoms have greatly improved or disappeared, the mental disturbance still persists.

Ligation of the vessels, whether internal carotid or vertebral, can hardly result in a cure. Only an amelioration of the signs and symptoms can be expected, and doubtless even this cannot be permanent. The precedent for such ligations is the treatment of arteriovenous aneurysms between the carotid artery and the cavernous sinus. Following ligation of the internal carotid for these traumatic aneurysms, there is much improvement but usually not a cure. The collateral supply through the circle of Willis militates against a cure; it is fair to presume the same free collateral circulation will preclude the cure of the intracranial aneurysms.

SUMMARY AND CONCLUSIONS

1. Eight arteriovenous aneurysms of the brain are presented from a series of tumors of the brain. Twenty-two additional cases have been assembled from the literature.

2. Arteriovenous aneurysms of the brain are similar to those of the vascular system elsewhere in the body, except that traumatic arteriovenous aneurysms probably do not occur in the brain, because large arterial and venous trunks are not in apposition.

3. There are two other types of arteriovenous aneurysms, one in which an anomalous vessel of congenital origin establishes a direct end

Aneurysms Collected from the Literature—Continued

| Head-ache | General Epilepsy | Focal Epilepsy | How Diagnosed | Diagnosis Before Operation or Autopsy | Operation and Observations | Conditions at Necropsy | Remarks |
|------------------------|------------------|-----------------|---------------|---------------------------------------|----------------------------|---|--|
| + | None | None | Necropsy | | | Enormous dilated veins on surface; tumor of entwined blood channels | There was much thrombosis with some evidence of cannalization; patient died of cerebral hemorrhage from attack |
| + | .. | + left side | Necropsy | | | Mass of vessels size of dove's egg below cortex right frontoparietal region; enlarged veins on surface of brain | Patient died of meningitis; calcareous deposits in vessels of vascular mass |
| .. | .. | .. | Necropsy | | | Specimen shows a large coiled vessel with many pouching dilatations; no note about veins | It is open to question whether this case is an arteriovenous aneurysm; patient died of cerebral hemorrhage (into ventricle) |
| .. | .. | + left face | | Epilepsy; later, aneurysm | | Left corpus callosum artery large and tortuous; right vena galeni parva and vena galeni magna large; tumor consists of mass of entwined vessels | Patient finally became demented; vessels of tumor did not seem either like normal veins or arteries; they were large cavernous spaces |
| .. | .. | .. | Necropsy | | | Mass of blood vessels in brain | Drawing of vessels suggests arteriovenous aneurysm |
| .. | .. | + right | Necropsy | | | Mass of vessels deep in corpus striatum; extends into ventricle at caudate nucleus; connection with choroid plexus vessels | When 10 years old patient suddenly developed weakness of right arm and leg; then improved and became stationary for 20 years when paralyzed anew; 114 years later coma and death from cerebral hemorrhage |
| None | None | None | Necropsy | | | Mass of small vessels in rolandic area | Patient died of cerebral hemorrhage; this lesion may or may not be an arteriovenous aneurysm; it has been described as a cavernous angioma |
| .. | .. | + right side | | | | Hemorrhage into ventricle and subarachnoid space; tumor of vessels 6 by 3 cm. in frontal region | When 10 years old hemiplegia suddenly developed on the right side with speech disturbance; gradual return of function and stationary condition for 21 years when paralysis and later convulsions developed |
| + localized in back | No | No | Necropsy | | | Vascular bed of vessels in right cerebellar lobe, anterior and posterior inferior cerebellar arteries run into angioma | Death from hemorrhage; much calcification and thrombosis in vessels |
| .. | .. | .. | Necropsy | | | Large surface veins; collection of vessels in parietal lobe projects into ventricle | Accidental finding at necropsy following operation for sarcoma of jaw; extensive thrombosis of cortical veins even of longitudinal sinuses; dilated venous trunks are localized to region draining angioma |
| .. | .. | .. | Necropsy | | | | This article is written in the Russian language but apparently there are two independent intracranial arteriovenous aneurysms; photographs appear to establish the lesion as arteriovenous |

LIGATION OF ARTERY AND CONCOMITANT VEIN IN OPERATIONS ON THE LARGE BLOOD VESSELS*

FRANK V. THEIS, M.D.

Resident Surgeon of the Presbyterian Hospital of Chicago
CHICAGO.

The beneficial effect of occluding the satellite vein when ligation of the artery becomes necessary in surgical conditions of the large blood vessels was first recognized by Sir Arthur Makins¹ in 1913. He found a lessened incidence of gangrene in following this procedure. Nevertheless, during the early part of the World War, careful preservation of the vein was practiced, but the occurrence of gangrene following ligation of the large artery to the extremity brought forth interesting and valuable investigations on the subject. Drummond² showed experimentally that ligation of both artery and vein produced "little or no change" in the condition of the loops of cat's intestines. When the artery alone was occluded, definite gangrene of the segment usually appeared within twenty-four hours. Van Kend³ attributed the decreased frequency of gangrene to a "slight rise in the blood pressure in the limb following application of a ligature to a vein, after previous ligature of the artery." He demonstrated this rise in blood pressure with plethysmographic tracings. With these and other reports presented at the Inter-Allied Conference of Surgeons in Paris, in May, 1917,⁴ the conclusion was reached that "facts tend to prove, even when the wound is limited to the artery, that simultaneous occlusion of the unwounded vein is to be recommended." The subsequent application of this procedure in the surgical treatment of arteriovenous aneurysms still further strengthens its clinical advantages.⁵

Application of the principle of ligation of the vein in cases of spontaneous gangrene seems to be gaining increased favor as evidenced by its more frequent mention in the surgical literature. In most of these

* From the Surgical Department of the Presbyterian Hospital and Rush Medical College of the University of Chicago.

1. Makins, Sir Arthur: *Gunshot Injuries to the Blood Vessels*, New York, William Woods & Company, 1919.

2. Drummond, Hamilton, quoted by Halsted: *Johns Hopkins Hosp. Rep.* 21: 1, 1921; quoted by Makins (footnote 1).

3. Van Kend, M., quoted by Makins (footnote 1).

4. *Compt. rend. Conf. Chir. Interall., Paris*, 1917.

5. Halsted, W. S., *Johns Hopkins Hosp. Rep.* 21:1, 1921. Holman, Emil: *Ann. Surg.* 85:173 (Feb.) 1927.

to end communication between an artery and vein; the other in which a network of vessels—a so-called angioma—is interposed between an artery and one or several veins. A capillary bed between the artery and vein is lacking in both types; the arterial blood, therefore, passes directly into the veins.

4. Both types are evident by the large, full and tortuous veins on the surface of the brain. A thrill can usually be felt, and red arterial blood can be seen pumping into the dark venous blood. The observations make the diagnosis absolute. There are usually congenital abnormalities of the surface veins of the brain.

5. Arteriovenous aneurysms of the brain are not uncommon, occurring in about 1 per cent of a series of tumors of the brain. They are located in almost every part of the brain.

6. The symptoms are fairly uniform and characteristic. Jacksonian convulsions, followed by transient loss of sensation or motor power in the part affected by the convulsion, and a gradually progressive sensory or motor hemiplegia on the affected side, are the symptoms common to most of the aneurysms affecting the cerebral hemispheres. The symptoms are usually of many years' duration, often beginning in childhood and continuing into adult life; again, they frequently do not begin until after the thirtieth or fortieth year.

7. General pressure symptoms, like those of a tumor of the brain, do occur, but in a minority of cases.

8. Cerebral hemorrhages occurred in about 40 per cent of the cases. It is the principal cause of death.

9. Changes shown by the roentgen ray are at times helpful in making a diagnosis and occasionally are pathognomic. Ventriculography helps to determine the existence of a space-occupying lesion.

10. The treatment is of two types: (1) ligation of the entering arteries, with or without extirpation of the mass of vessels—so-called angioma; (2) ligation of the internal carotid artery (for cerebral aneurysm) or of the vertebral artery (for cerebellar aneurysm). Occasionally, a subtemporal or cerebellar decompression (depending on the location of the aneurysm) may be indicated.

Radical ligations or extirpations alone are curative, but are exceedingly dangerous to life and function and indicated in the minority of cases, when the aneurysm is posterior to the motor tracts.

With these conflicting reports in mind, two methods were used to study the collateral circulatory bed which develops when the main arterial supply of the limb is interfered with.

1. Roentgen-ray visualization of the vascular bed in:

- (a) Amputated lower extremities in which the vessels were pathologic.
- (b) The study of the lower limbs of experimental animals following ligation of the artery alone on the one side as compared to the ligation of the artery and vein on the other side. This study was made on different animals over various periods of time up to three months after the operations.
- (c) The effect on the visualization of the collateral circulation by varying the pressure of the injection of the opaque emulsion into the diseased vessels of the amputated limbs on the one hand, and the normal vessels of the animals, on the other.

2. Determinations of the volume of blood flow were made over various periods of time on the surviving experimental animal. The determinations were made from the distal open end of the ligated femoral artery below the profunda with and without simultaneous ligation of the vein.

ROENTGEN-RAY VISUALIZATION OF THE CIRCULATORY BED

Blood Vessels in Amputated Legs.—Roentgen-ray visualization of the circulatory bed was first used by Drummond² in his original work on ligation of the arteries and the veins. Meleney and Miller,¹⁴ in studying the collateral vascularity in amputated limbs for gangrene, were the first to publish its value, in a most comprehensive article. Lewis and Reichert¹⁵ also published a similar investigation with the use of bismuth oxychloride and acacia emulsion as the material for injection instead of the previously used barium. In my experiments I find that the bismuth emulsion as recommended by Hill¹⁶ gives the most perfect roentgenograms of the arterial tree and collaterals without diffusing into the surrounding tissues as is seen when sodium iodide solution is used. On the other hand, barium does not throw so dense a shadow as metallic mercury, and both of these are too coarse to fill the finer arterioles.

The outstanding roentgenograms of ten amputated limbs that I have studied are taken in two cases of thrombo-angiitis obliterans. The clinical histories in both cases were almost identical. In the one case, the patient was 50 years of age and of German descent. He had had symptoms of intermittent claudication, pain in the calf of the leg and discoloration and numbness of the right foot almost continuously for five years. The other patient was 48 years of age, a Russian Jew who had had similar symptoms for only two years. In both there was a complete absence of pulsation in the dorsalis pedis, posterior tibial and popliteal arteries. Even the results of the intracuticular salt solution

14. Meleney and Miller (footnote 9, sixth reference).

15. Lewis and Reichert (footnote 9, seventh reference).

16. Hill (footnote 9, eighth reference).

cases, however, there has been a previous gradual occlusion of the main artery to the extremity. In 1913, Oppel⁶ was the first to report improvement following ligation of the popliteal vein in six cases of threatened senile gangrene of the foot. He attributed the encouraging results to the retardation of the venous return flow and the consequent rise in the blood pressure of the limb. Stradin⁷ also employed ligation of the vein in cases of spontaneous gangrene, reporting good results, but he combined it with sympathectomy. McWhorter⁸ recently presented before his clinic at the Presbyterian Hospital, three cases of thrombo-angiitis obliterans with ligation of the femoral vein. Two of the patients had subsequent amputations, although the third showed encouraging improvement over a period of five months. As a result of experiments on animals, Brooks,⁹ Holman¹⁰ and Pease¹¹ have corroborative evidence for employing simultaneous ligation of the vein when the artery is occluded.

In reviewing the literature, however, I found that the final results of McNealy,¹² Thurston¹³ and others, who employed ligation of the femoral vein in cases of spontaneous gangrene, were discouraging. While the value of occluding the venous return flow may not be overestimated when sudden obstruction of the artery occurs, its further use in conditions of chronic occluding diseased processes in the arteries is of doubtful value.

6. Oppel: *Zentralbl. f. Chir.* **31**:1241, 1913.

7. Stradin, P.: *Deutsche Ztschr. f. Chir.* **194**:289 (Jan.) 1926.

8. McWhorter, Golder, L.: Personal observation and communication.

9. Brooks, Barney, and Martin, Kirley: *Simultaneous Ligation of the Vein and Artery*, J. A. M. A. **80**:1678 (June 9) 1923. Holman, Emil and Edwards, Muriel, *New Principle in Surgery of Large Vessel; Ligation of Vein Proximal to Site of Ligation of Artery*, J. A. M. A. **80**:909 (March 19) 1927. Pease, Herman: *Ann. Surg.* **86**:850 (Dec.) 1927. McNealy: *Surg. Gynec. Obst.* **40**:45 (Jan.) 1925. Thurston, J. A.: *Bull. U. S. Vet. Bur. Med.* **1**:1 (Dec.) 1925. Meleney and Miller: *Ann. Surg.* **81**:976, 1925. Lewis and Reichert: *Collateral Circulation in Thrombo-Angiitis Obliterans; Indication for Ligation of Femoral Artery First Distal to Profunda*, J. A. M. A. **87**:302 (July 31) 1926. Hill, E. E.: *Bull. Johns Hopkins Hosp.* **35**:318, 1924. Halstead (footnote 5, first reference). Holman (footnote 5, second reference). Schrt, E.: *Med klin.* **12**:1338, 1916. Stern and Cohen: *Intracutaneous Salt Solution Wheal Test; Its Value in Disturbances of Circulation in Extremities*, J. A. M. A. **87**:1355 (Oct. 23) 1926. Brooks and Jostes: *Clinical Study of Diseases of the Circulation of the Extremities: Description of a New Method of Examination*, *Arch. Surg.* **9**:485 (Nov.) 1924.

10. Holman (footnote 9, second reference).

11. Pease (footnote 9, third reference).

12. McNealy (footnote 9, fourth reference).

13. Thurston (footnote 9, fifth reference).

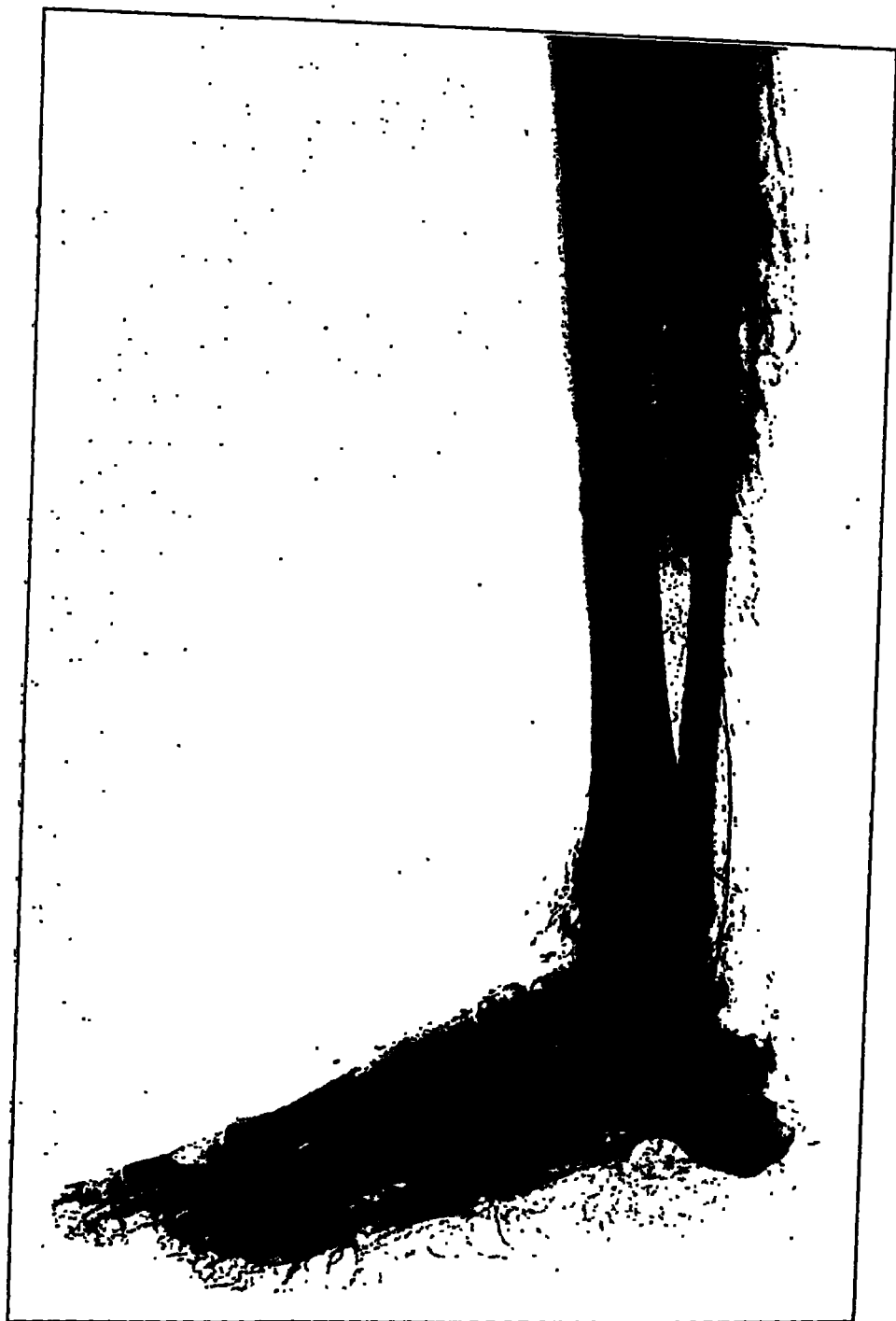


Fig. 1.—Roentgen-ray visualization of the vascular bed in leg amputated for thrombo-angiitis obliterans. Note the extensive collateral vascular bed with almost complete occlusion of the main arteries.

test¹⁷ were exactly similar, indicating the same degree of apparent circulatory deficiency—the wheals disappearing within from five seconds on the great toe to one hour plus on the thigh. In the first case, amputation was performed because of rapidly spreading gangrene with infection; in the second, because of the extreme unremitting pain in the calf of the leg, but no gangrene. Microscopic and macroscopic examination of the arteries confirmed the diagnosis and showed almost the same degree of involvement. After injection of the popliteal artery in each case, roentgen-ray visualization revealed an extensive collateral vascular bed to account for the absence of gangrene in the one case (fig. 1), while in the other, with a much longer duration of the symptoms, an almost complete absence of the collateral vessels was found. This suggested the probability that there might be some controllable factors which could increase the formation of collateral vessels in cases of this kind.

Vascular Bed in Experimental Animals After Ligation of the Superficial Femoral Artery, With and Without Simultaneous Occlusion of the Common Iliac Vein.—Ten experiments on animal were carried out to determine the effect on the collateral circulatory bed of ligating the proximal satellite vein with the artery as compared to the ligation of the artery alone. The superficial femoral artery was ligated just below the profunda femoris on both sides, but in addition, the common iliac vein was simultaneously ligated on the right side. The animals were killed at various periods, from immediately after to three months after operation. The abdominal aorta was then injected with the bismuth oxychloride emulsion under a pressure of 125 mm. of mercury. Roentgen-ray visualization immediately after the operation showed the collateral vascular bed to be best where both the artery and the vein were ligated (fig. 2). In three weeks, however, the vascular bed was more developed where the artery alone was occluded, as compared to the opposite side where the common iliac vein was occluded simultaneously with the artery (figs. 3 and 4).

Vascular Bed During Variation in the Pressure of the Injections. The much discussed influence of elevating the blood pressure in certain cases of circulatory deficiency due to peripheral arterial disease suggested the study of the vascular bed with variation in the pressure of injection of the extremities. Amputated limbs were first injected with a manometer pressure of around 150 mm. of mercury, the patient's own blood pressure (fig. 5). Roentgenograms were then taken and the limbs reinjected with double the pressure (300 mm. of mercury) (fig. 6). Only the faintest improvement in the finer arterioles could be detected even with such a marked increase in pressure. Further increase of pressure, however, improved the bed considerably. This probably

17. Stern and Cohen (footnote 9, ninth reference).

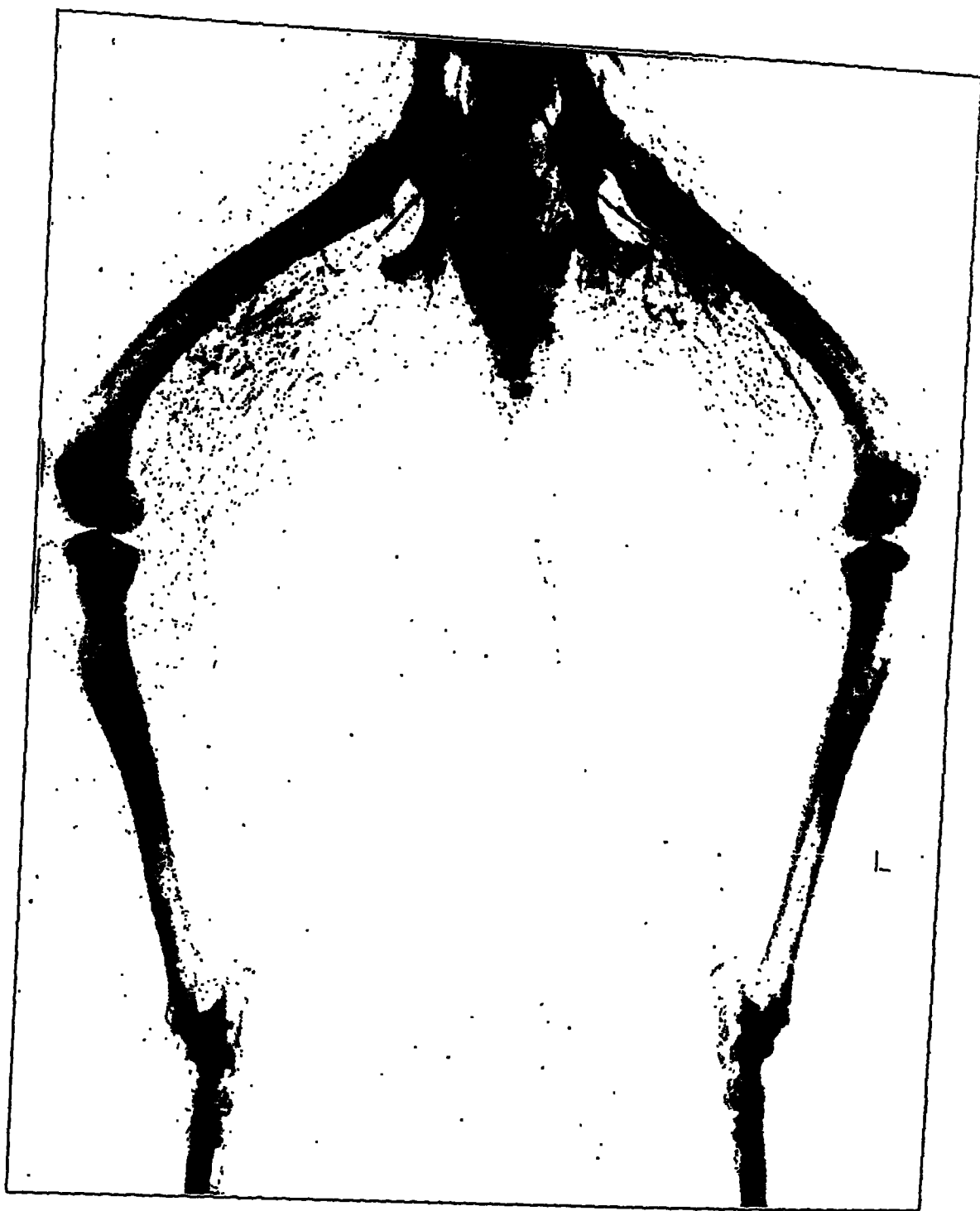


Fig. 3.—The vascular bed of the lower extremities of an animal three weeks after operation shows equal development on both sides. On the right leg the artery and vein were simultaneously occluded while on the left only the femoral artery was ligated. Note the large obturator arteries which are now the main source of arterial supply to the extremities.

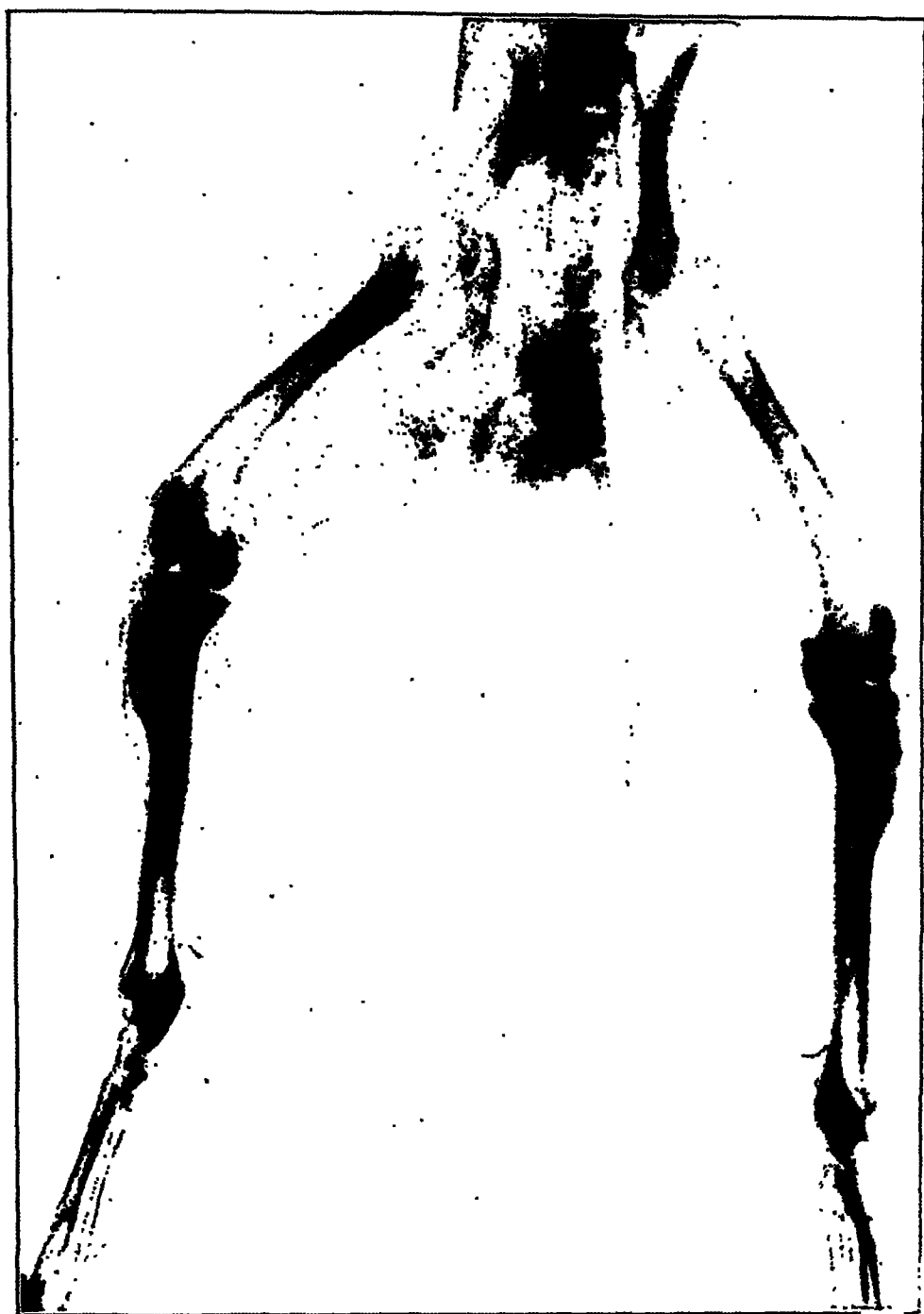


Fig. 2.—Roentgen-ray visualization with injection of the abdominal aorta under a pressure of 125 mm. of mercury immediately after operation. The collateral vascular bed is seen to be more developed where the artery and concomitant vein have been simultaneously ligated (left side of picture).

accounts for some of the excellent roentgenograms that are frequently seen when an accurate check is not made to determine the pressure back of the injection. In order to eliminate the postmortem changes as much as possible, the limbs were studied immediately after amputation.

Considering the slight rise in blood pressure and the clinical advantage of simultaneous ligation of the satellite vein with the artery, the effect of moderate variations in the pressure of the injected material on the normal vessels of experimental animals was next studied. In order to bring out the collateral vascular bed of the nonpathologic arterial tree, the superficial femoral artery on both sides was occluded. The animal was killed, and the abdominal aorta was injected with the opaque mass under a pressure of 100 mm. and 150 mm. of mercury, and roentgenograms were made after each injection. In contrast to the slight improvement seen when the vessels were pathologic, the normal vessels showed marked improvement of the collateral bed when the pressure of the injection was increased. No doubt this difference was due to the fact that the elasticity of the artery is lost in the diseased vessel.

Determinations of the Volume of Blood Flow With and Without Ligation of the Concomitant Vein.—The temporary immediate improvement of the collateral circulatory bed with concomitant ligation of the vein as was seen in the roentgen-ray visualizations suggested the advisability of determining the volume of blood flow over a period of weeks in surviving experimental animals. This was next studied on dogs at twenty operations.

EXPERIMENTAL WORK

Large male dogs were used. Under a light ether anesthesia, the right superficial femoral artery was isolated. After a temporary distal ligature was applied, a citrated 18 gage transfusion cannula was inserted proximally into the artery. The normal flow averaged about 240 cc. per minute. The flow in each case was obtained for from five to ten seconds, and the minute determination calculated therefrom. When the cannula was removed a ligature was applied proximal to the opening in the artery, and the cannula was reinserted distally. Through an incision over the lower right rectus muscle, a previously introduced ligature around the common iliac vein was tied. The immediate flow per minute from the distal end of the ligated artery was 48 cc.; in ten minutes it was the same, in thirty minutes, 51 cc., and in one hour, 54 cc. Three weeks later, the same procedure was followed on the left femoral artery, but without occlusion of the common iliac vein. The normal proximal flow was found to be the same as on the right side. From the distal end of the ligated artery, the flow immediately following the ligation was 39 cc., increasing to 42 cc. in ten minutes, 48 cc. in thirty minutes, and 54 cc. in one hour. At the same operation, the distal end of the ligated right femoral artery of the previous operation was again isolated and cannulized. The flow was found to be 96 cc. per minute, having increased from 54 cc. during the three week interval. The distal end of the left femoral artery was recannulized at a subsequent operation three weeks later, and was found to have increased from 54 to 136 cc. per minute. All the factors, including the depth of the ether anesthesia were kept as constant as possible. No more than 50 cc. of blood was withdrawn at one operation.

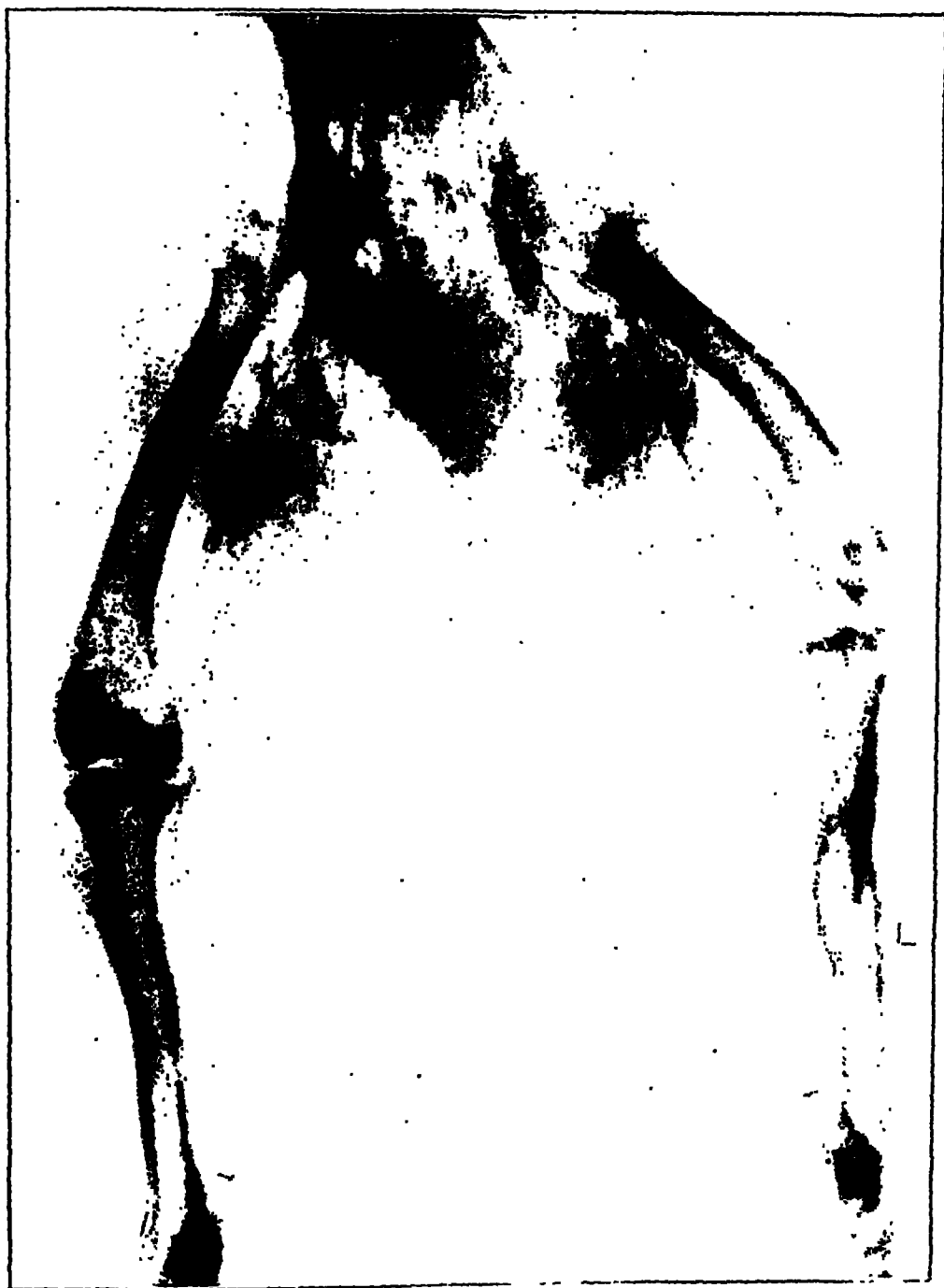


Fig. 4.—Six weeks after operation the vascular bed shows greater development on the left leg where the artery alone has been ligated as compared to the right side with both artery and vein occluded.

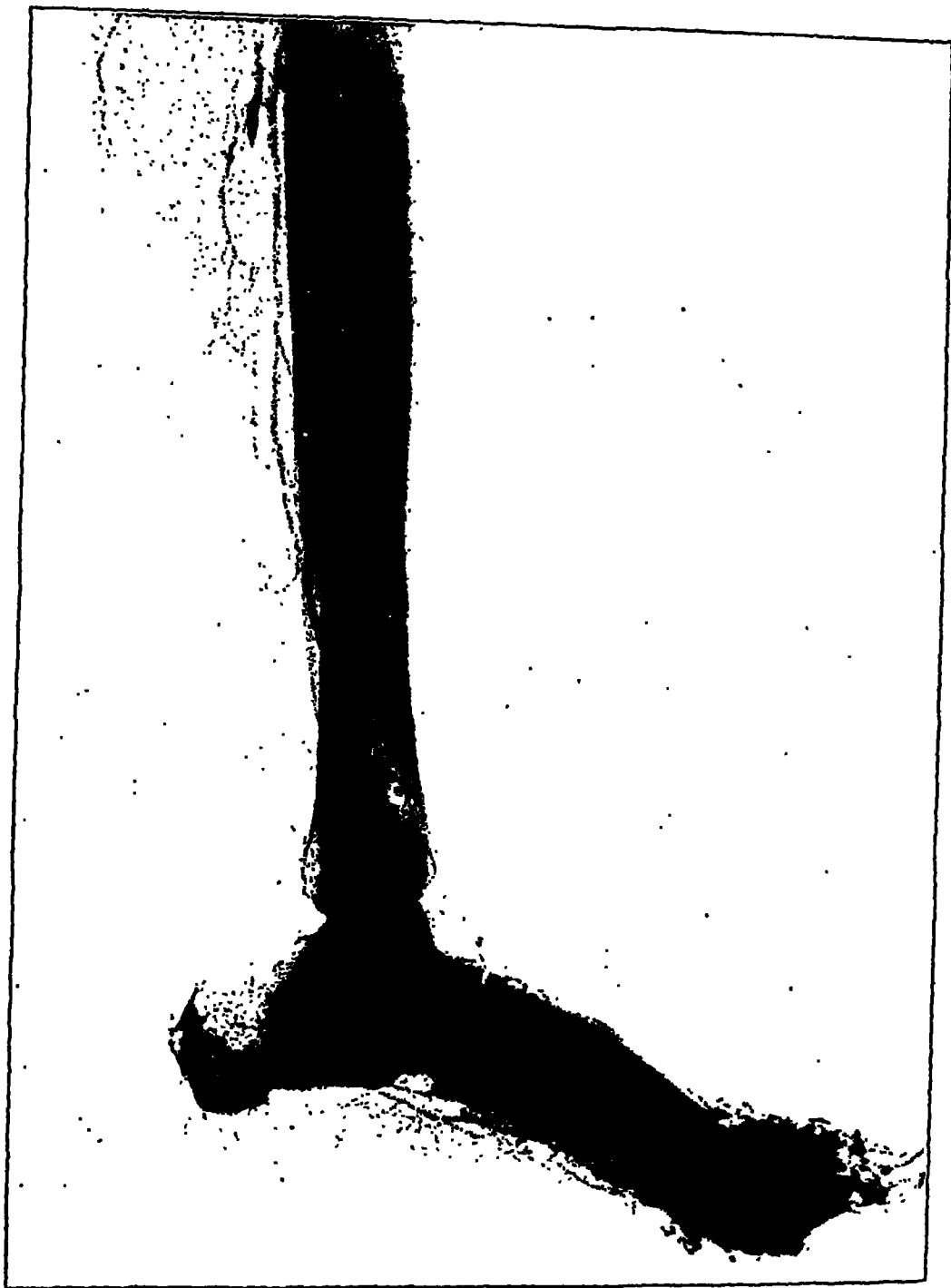


Fig. 6.—Same limb as in figure 5 with reinjection under a pressure of 300 mm. of mercury. Note that even with double the pressure only the faintest improvement in the collateral vascular bed can be detected.

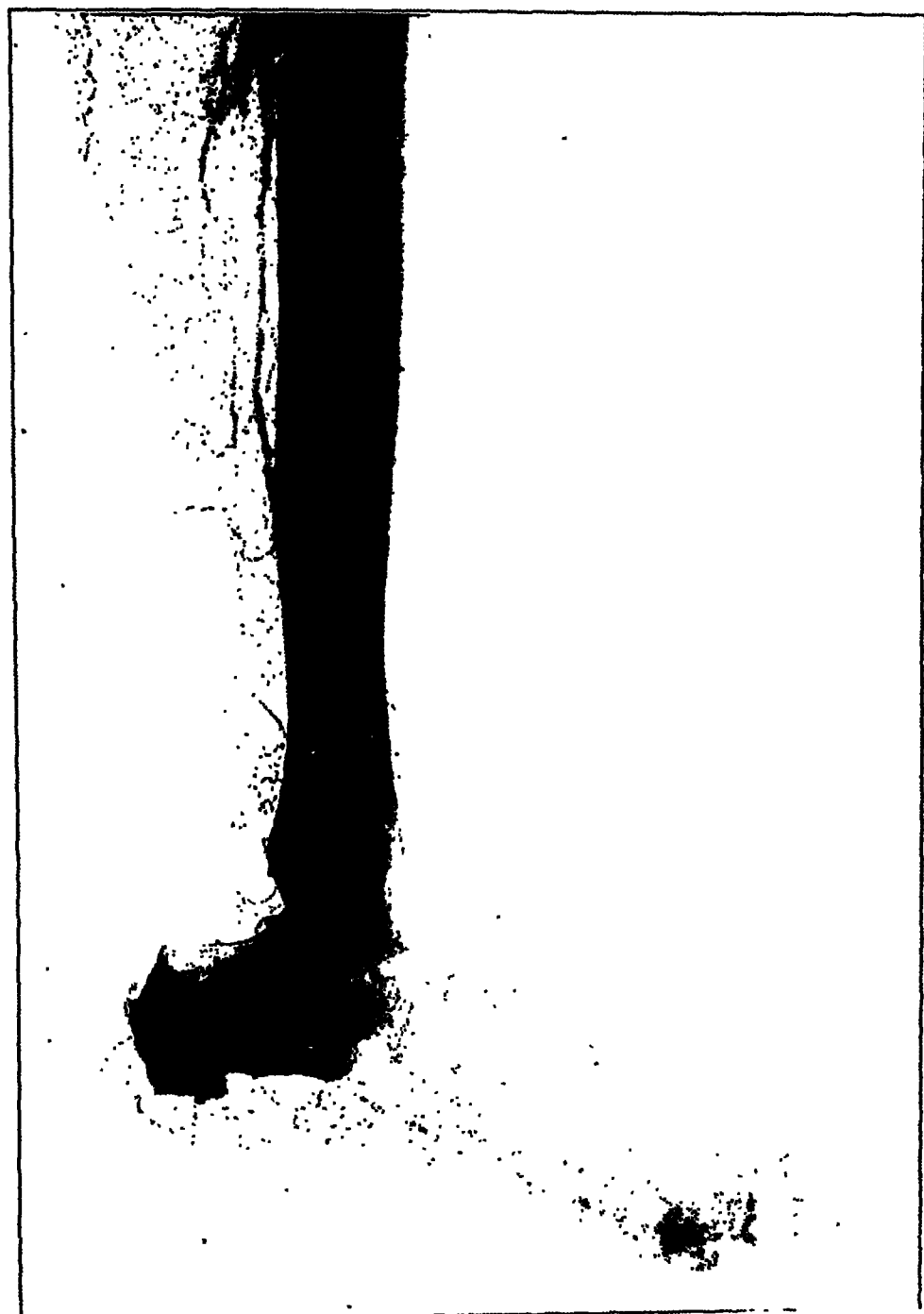


Fig. 5.—Amputated limb with the injection of the opaque mass under a pressure of 150 mm. of mercury.

Results.—Immediate transitory increase in flow from the distal end of the ligated femoral artery was obtained where the proximal concomitant vein was simultaneously occluded.

In the experiments in which the artery alone was ligated, this temporary increase was overcome and exceeded within one hour in all the animals. Moreover, when the artery alone was ligated, in one of the animals the normal flow as previously determined from the proximal end of the ligated artery returned within six weeks (fig. 7).

*Determination of Blood Volume Flow in Cubic Centimeters on Dogs **

| Dog | Normal | Immed. Oc. | Minutes | | | | | Weeks | | | |
|------|--------|---------------|---------|----|----|----|----|-------|----|-----|-----|
| | | | 10 | 20 | 30 | 40 | 60 | 2 | 3 | 4 | 6 |
| I | R— | 30 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| | L— | 25 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| II | R— | 20 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| | L— | 20 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| III | R— | 10 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| | L— | 14 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| IV | R— | 10 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| | L— | 9 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| V | R— | 15 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| | L— | 12 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| VI | R— | 14 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| | L— | 12 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| VII | R— | 32 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| | L— | 32 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| VIII | R— | 12 | .. | .. | .. | .. | .. | .. | 21 | .. | .. |
| | L— | 12 | .. | .. | .. | .. | .. | .. | 48 | .. | .. |
| IX | R— | 14 | .. | .. | .. | .. | .. | 32 | .. | .. | .. |
| | L— | 11 | .. | .. | .. | .. | .. | 42 | .. | .. | .. |
| X | R— | 22 | .. | .. | .. | .. | .. | .. | .. | .. | 52 |
| | L— | 20 | .. | .. | .. | .. | .. | .. | .. | .. | 63 |
| XI | R—220 | 16 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| | L—220 | 12 | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| XII | R—190 | 48 | 48 | .. | 48 | .. | .. | .. | .. | 66 | .. |
| | L—220 | 42 | 42 | .. | .. | 54 | 60 | .. | .. | 90 | .. |
| XIII | R—264 | 80 | 80 | 90 | 90 | .. | .. | .. | .. | .. | ? |
| | L—240 | 72 | 48 | 51 | 54 | .. | .. | .. | .. | .. | 210 |
| XIV | R—240 | 18 | 18 | .. | 24 | .. | 24 | .. | .. | .. | 36 |
| | L—240 | 15 | 18 | .. | 21 | .. | 24 | .. | .. | .. | 42 |
| XV | R—240 | 48 | 48 | .. | 51 | .. | 54 | .. | .. | 96 | .. |
| | L—252 | 39 | 42 | .. | 48 | .. | 54 | .. | .. | 120 | .. |

* The left superficial femoral artery was ligated alone while on the right side the common iliac vein was simultaneously ligated with the artery. The normal flow was obtained by cannulizing the proximal end of the ligated artery, and the other determinations were made from the distal end. The flow was obtained for from five to ten seconds and the minute volume determinations calculated from the amounts obtained.

Pulsation in the distal part of the artery returned somewhat more slowly but to a final greater volume when the vein was left patent. This is in accord with the determinations of the blood flow shown in the table.

Atrophy, disability or gangrene did not develop following ligation of the superficial femoral artery, irrespective of the patency of the vein. In most cases, the circulation was decreased to below 10 per cent of normal.

COMMENT

The slight increase in the residuary arterial pressure after ligation of the artery and concomitant vein, as found by Van Kend, Brooks, Holman and Pease, must be a deciding factor in the immediate transitory improvement in the blood flow when the blood vessels are normal.



Fig. 7.—The left superficial femoral artery was ligated alone. After previous determination of the normal volume flow from the proximal end of the artery, six weeks later at subsequent operation, exactly the same flow was obtained distal to the ligation. Not in the roentgen-ray visualization the extensive development of the collateral bed which practically equals that on the right side where the circulation had not been disturbed!

With the gradual occlusion of the arterial tree that has already taken place in cases of threatened gangrene of the extremities from arterial disease, less benefit would be derived from the initial improvement following proximal ligation of the satellite vein. In these cases, the collateral vessels have had an opportunity to develop during the time that the main artery had become occluded. It is then probable that the ordinary course of events are insufficient to open the potential collaterals. The principle of ligation of a proximal satellite vein is neither applicable nor warranted as a surgical procedure in cases of spontaneous gangrene resulting from arteriosclerosis or thrombo-angiitis obliterans.

When the final maximum increase in the collateral vascular bed rather than immediate improvement is necessary, as in cases of thrombo-angiitis obliterans and other forms of threatened gangrene, ligation of the artery alone is to be recommended. Both on experimental grounds and clinically, as advocated by Lewis and Reichert,¹⁵ this procedure is most likely to give the best results.

CONCLUSIONS

The results of the determinations of the volume of flow and the study of the injected collateral vascular bed in experimental animals show that the final increase in collateral vessels is far better when the vein is patent.

With sudden occlusion of a large artery, as in embolism or injury to the vessel, the immediate improvement in the collateral bed due to ligation of the concomitant vein is needed to maintain the vitality of the limb.

When a certain amount of collateral vessels have had an opportunity to develop, as in threatened spontaneous gangrene, surgical procedures on the main vessels of the extremities should be limited to the artery alone.

Contrary to the results reported by Holman, Brooks and others, my experiments show that the increased volume of flow with the artery and the proximal main vein ligated is only slight and transitory. After the initial improvement, there is a retardation of the volume of flow in the subsequent determinations as compared to the increase occurring on the side where the artery alone is occluded.

During the World War, ligation of the artery alone for aneurysm of the femoral artery in surgical procedures was followed by gangrene in more than 50 per cent of the cases. In experiments on dogs and rabbits, Brooks¹⁸ reported the occurrence of gangrene in 71.5 per cent of the animals in which the artery alone was occluded and in 33.3 per cent in which both the artery and the satellite vein were ligated. In both instances, the femoral artery was ligated at the same level. Sehrt¹⁹ reported 20 and 9 per cent of gangrene respectively, with ligation of the femoral artery, and with simultaneous ligation of the femoral artery and vein. Irrespective of the site of the occlusion of the femoral artery, gangrene occurred less frequently when both artery and vein were occluded. Clinically, one sees gangrene develop following embolism of the popliteal artery, but not necessarily when the arterial occlusion is more gradual as in many cases of arteriosclerosis and thrombo-angiitis obliterans. Although in my series of experiments on dog, atrophy or gangrene failed to develop with occlusion of the superficial femoral artery below the profunda with or without simultaneous ligation of the common iliac vein, the ability of the collateral vascular bed to develop sufficiently rapidly is of more importance as a cause of gangrene than the point of occlusion of the artery.

The practice of ligation of the artery and the concomitant vein in traumatic surgical procedures, especially in the treatment of patients with arteriovenous aneurysm, is recognized to be of great clinical value. Experimentally, it has been impossible to confirm the enormous improvement with ligation of the artery and the proximal vein as found by Holman.¹⁰ The difference in the results may be due to the fact that his work was done on rabbits over a short period of time and with the use of a noncoagulant in the blood. However, roentgen-ray visualization soon after the operation showed the most marked development of the vascular bed where the vein had been simultaneously occluded (fig. 2). Singularly enough, this immediate temporary benefit following simultaneous occlusion of the satellite vein in cases of sudden arterial obstruction may be the deciding factor in maintaining the vitality of the limb, the absence of which predisposes to the frequent occurrence of gangrene.

18. Brooks (footnote 9, first reference).

19. Sehrt (footnote 9, tenth reference).

are multiple in both kidneys, and the symptoms and shape of the stones warrant surgical intervention, every effort should be made to preserve renal tissue.

The patient's age may also be a factor in determining the operative procedure. In a case of unilateral multiple stones in an old person nephrectomy may be advisable, whereas a similar condition in a young person might warrant conservative operation. If a patient more than 60 years of age has a renal stone that is causing few or no symptoms, the stone may be left; if the patient were younger, removal would be indicated.

DIFFERENTIAL RENAL FUNCTION

The comparative estimation of function of either kidney by present methods is notoriously uncertain and misleading. Because of reflex irritation caused by the presence of stone in the renal tissue, the tests of function are frequently inaccurate. It has been our experience that reliance can be placed only on high and low values. The normal or nearly normal return of dye from the affected kidney can be accepted as an accurate index of the condition. No return of dye, or only a trace, usually indicates marked destruction of renal tissue, although in some cases a surprising amount of good renal tissue is found at operation. Intermediate values of dye return are inaccurate, and little reliance can be placed on their interpretation.

Intravenous injection with indigo carmine is the simplest functional method. The intensity of the color of the urine from either ureteral orifice affords a rough but fair index of the renal function. The differential phenolsulphonphthalein test is usually more accurate in determining the degree of reduction in function, but is equally subject to reflex inhibition of secretion and to technical error because of leakage around the ureteral catheter and faulty drainage. Nevertheless, in determining the type of operation in cases of multiple stones, especially of bilateral nephrolithiasis, differential renal functional tests may be of decisive practical value. Pyelography may be more accurate in giving an estimate of renal function than any dye test by outlining the extent and character of the pyelectasis or other deformity. In other words, extensive destruction of renal tissue is rare when the pyelogram demonstrates a comparatively normal pelvis. However, if there is evidence of marked pyelectasis, elongation and dilatation of all calices, cortical necrosis, cicatricial changes, or marked atrophy of the renal pelvis, renal injury is usually considerable, and nephrectomy may often be desirable.

RENAL FLUOROSCOPY

There is no preoperative diagnostic method which will always enable one to determine the exact number of stones present, even though shadows visible in the roentgenogram may be identified as intrarenal.

MULTIPLE RENAL STONES

PROBLEMS IN THE TREATMENT OF PATIENTS WITH THIS CONDITION

WILLIAM F. BRAASCH, M.D.

AND

JOHN L. CULLIGAN, M.D.

Fellow in Urology, The Mayo Foundation

ROCHESTER, MINN.

The indications for operation in the presence of multiple stones in the kidney are not standardized and are influenced largely by the clinical data in the individual case. The tendency in recent years has been toward conservation. If in the complete removal of stones the kidney is not too greatly injured, and if it is shown that considerable function remains, the kidney should be saved. It may be comparatively easy to remove the kidney, but it requires experience and the cooperation of several technical aids to remove all the stones successfully and save the kidney. Among the factors which must be considered in determining the advisability of conservative operation are the size, shape and number of stones, the area involved, the function of the organ and the age of the patient.

SIZE AND SHAPE OF STONES

It should be recognized that the removal of large branched stones may necessitate considerable destruction of renal tissue. The removal of round, smooth stones, even if they are of considerable size, causes much less injury than removal of branched or coraliform stones which fill the pelvis and calices. Round stones are usually situated in the pelvis and seldom involve the calices; therefore their removal by pelvolithotomy is usually comparatively easy. If a branched stone involves but one calix, destruction of renal tissue resulting from its removal is not extensive. When, however, all the calices are involved, complete removal of the stones from the ends of the calices usually causes so much destruction of renal tissue that conservation is inadvisable. The complete removal of multiple small stones situated in different portions of the kidney without much injury to the renal tissue is difficult because of failure of localization. Such difficulty is greatly lessened by the aid of renal fluoroscopy. The suggestion made by W. J. Mayo and by Geraghty that large branched stones in both kidneys should be left alone unless the symptoms are so acute as to warrant emergency operation is, in general, followed. In cases of round or smooth stones in both kidneys, however, operative results are usually much better. If stones

course of six months or may not change in a year or two. They are often not due to actual lithiasis, but to deposits of calcium in the tissues, sandy material, pieces of adhesive plaster near the external wound or bits of suture. In case small fragments remain, drainage is usually well established, and they are often passed spontaneously. In two cases in which the kidney was incompletely delivered, definite shadows of stones of 1 cm. in diameter were noted in the postoperative roentgenograms of partially delivered kidneys. It is in these cases that renal films exposed at operation as suggested by Quinby would be particularly valuable. Although this method is simpler and is more widely available, the delay in developing the films and the technical errors which may arise will retard the operation. Furthermore, localization of the stone is much less accurate.

As previously stated, the indications for operation in cases of multiple renal stones vary largely with the individual circumstances. The following cases are illustrative of many of the problems that present themselves.

REPORT OF CASES

CASE 1.—Multiple stones in one kidney and stone in the lower portion of the ureter on the same side.

A man, aged 27, complained of having had repeated colic referred to the left loin for several years. Results of physical examination at the clinic were negative. Urinalysis showed 35 pus cells to a field. The renal functional tests were normal. Roentgenograms disclosed the shadow of a branched stone or possibly multiple stones in the area of the left kidney; also two shadows in the region of the lower portion of the left ureter, the larger shadow measuring 1.5 by 1 cm., and the smaller 1 by 1 cm. On cystoscopy, an impassable obstruction was encountered in the left ureter at the ureterovesical juncture. The dye tests indicated moderate reduction in function of the left kidney. The right kidney was normal. The operative procedure consisted of preliminary left ureterolithotomy followed several weeks later by nephrolithotomy with removal of a branched stone and several fragments.

Comment.—If stones are present in both ureter and kidney on the same side, it is usually first advisable to remove the stone from the ureter. It has been our experience that a ureteral stone will frequently be displaced immediately following operation on the kidney and may then cause a complicating ureteral obstruction. If the stone is small and situated at the wall of the bladder, manipulation might first be tried although with stones in the kidney as well, only one or two attempts should be made because of possible complicating acute pyelonephritis. With multiple stones of this size ureterolithotomy rather than cystoscopic manipulation is indicated.

CASE 2.—Stone in the kidney and migratory stone in the ureter on the same side.

A woman, aged 36, had had intermittent pain referred to the right lower quadrant of the abdomen for three years. Physical examination was negative.

It is now generally recognized that the number of stones discovered at operation often differs from the number of shadows in the roentgenogram; therefore, a method must be employed which will ensure complete removal. Two procedures employed to accomplish this are renal fluoroscopy and roentgenograms made on the operating table. In fact, it is questionable whether a conservative operation for multiple renal stones should be attempted without using one of these methods. We have employed renal fluoroscopy in 370 cases and have found it most useful in the removal of multiple renal stones. Those who are not experienced in the use of renal fluoroscopy claim that it often fails because it does not reveal all the stones. This may occasionally be true of minute fragments from 1 to 2 mm. in diameter. It is rarely true of stones larger than from 2 to 3 mm., if correct technic is employed. Another objection may be raised because of the difficulty experienced in the exact localization of small stones, but this procedure may be greatly aided by the insertion of needles at different angles, under the guidance of the fluoroscope, so that the needle points will approximate at the site of the stone. The objection has been raised that the surgeon is placed in an awkward position when there is a small stone in the end of a calix or in the parenchyma which in spite of skill and patience he is unable to find. As a result, either considerable mutilation of the kidney may be necessary before the stone is found and removed, or it may be advisable to remove the kidney rather than to let the stone remain. There are limits to the extent of renal injury justified in searching for a fragment of stone, and it may occasionally be advisable to leave a small stone fragment rather than injure the kidney further. We have observed several cases in which a small stone was left pocketed at the end of a calix after multiple stones had been removed from the kidney, and on reexamination years later, the stone had not increased in size, had not caused symptoms, and the function of the kidney was almost normal. Leaving the stone, however, is justifiable only in selected cases of this kind. It is true that unless the kidney can be delivered above the level of the abdominal wall, it may be difficult to see it clearly, and yet if the patient is thin, it is remarkable how clearly the kidney can be seen even though not completely delivered. This difficulty has been observed in approximately 15 per cent of all cases.

No method of diagnosis is infallible, but in a review of the 370 cases of renal lithiasis in which renal fluoroscopy was employed, we have found shadows in postoperative roentgenograms in only 21 cases or 6 per cent. In most of these cases, the kidney was incompletely delivered. In several cases, the shadows were doubtful. In fact, minute shadows of no surgical significance are not infrequently observed in the roentgenogram taken soon after operation. Such shadows may or may not be associated with any symptoms and may either disappear in the

figure 1, the shadows of the two stones are visible. one in the right kidney and the other in the right ureter at the level of the third lumbar vertebra.

CASE 3.—*Stone in the kidney and pyonephrosis, and stone in the lower portion of the ureter, indicating nephro-ureterectomy.*

A man, aged 22, gave a history of recent attacks of pain referred to the upper part of the left side of the abdomen, with pyuria and hematuria. Physical examination revealed tenderness over the area of the left kidney. The phenol-



Fig. 2 (case 3).—Multiple stones in the left kidney and lower portion of the left ureter.

sulphonphthalein return was 45 per cent in two hours. The urine contained large quantities of blood and pus. On cystoscopic examination, there was evidence of marked reduction in function of the left kidney and an obstruction impassable to the catheter in the lower portion of the left ureter. Roentgenograms disclosed multiple scattered branched stones in the area of the left kidney and multiple large stones in the lower portion of the left ureter. An anterior incision was made, and the lower end of the ureter was freed and ligated. Later nephrectomy was performed through a lateral incision, and the ureter was drawn out with the kidney.

Urinalysis was negative save for a few pus cells. Roentgenograms showed one shadow 1 cm. in diameter in the area of the right kidney and another 1.5 cm. in diameter in the region of the right ureter at the level of the fifth lumbar vertebra. Unsuccessful attempts were made to remove the ureteral stone by manipulation. It was then decided to displace it upward by means of a ureteral catheter introduced through the cystoscope so that both stones could be removed through the same incision at operation. This was done while the patient was under anesthetic just before the incision was made over the area of the right kidney. Pelviolithotomy was then performed, with removal of both stones through the same incision.

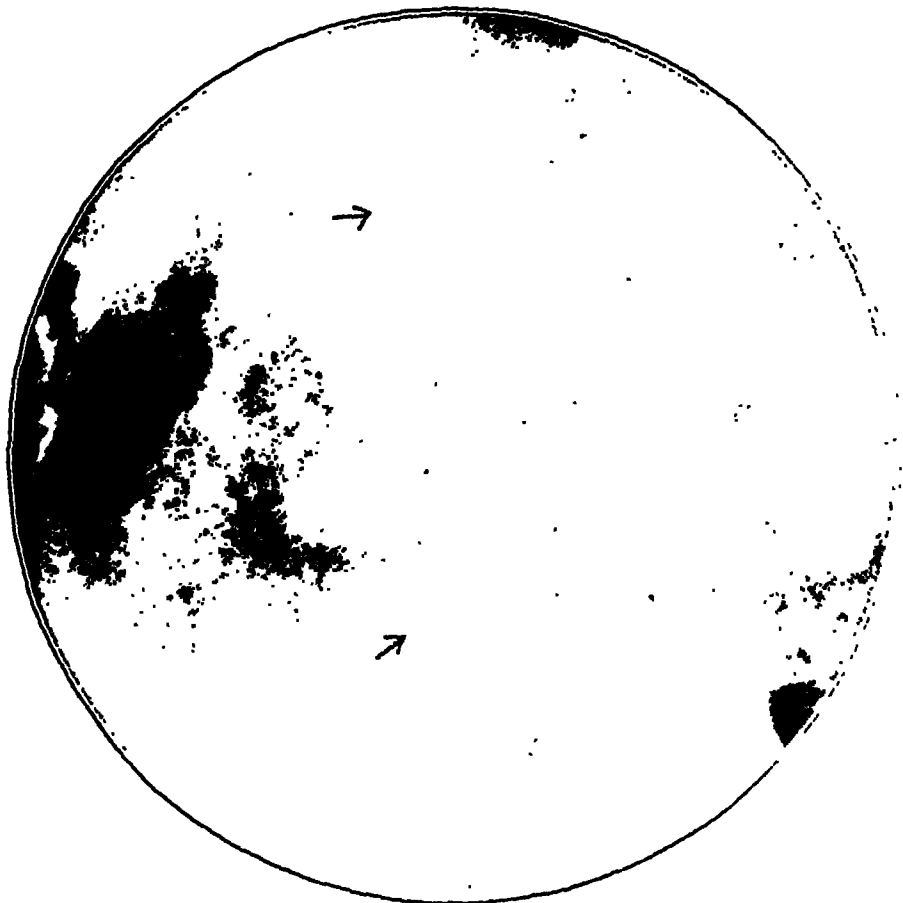


Fig. 1. (case 2).—Two stones, one in the right kidney and the other in the right ureter at the level of the third lumbar vertebra.

Comment.—The patient was saved from the ordeal of a possible second operation by this simple maneuver. It is evident that such manipulation would be possible only with a migratory stone and in the presence of a dilated ureter. Removal of a stone situated in the upper third of the ureter by means of the usual methods of ureteral dilatation is usually difficult and possible of accomplishment only after repeated trials and long delay. In the presence of two stones favorably situated the operative procedure here employed is usually to be preferred.

CASE 5.—Massive bilateral nephrolithiasis, symptomless and inoperable.

A man, aged 20, gave a history of a slight dull ache in the right side of the abdomen for the last six months. There were no urinary symptoms. Results of physical examination were negative, except that urinalysis disclosed 40 pus cells to a field. Roentgenograms showed massive multiple stones in the areas of both kidneys and a single stone in the area of the bladder. The phenolsulphonphthalein output was 35 per cent in two hours, the blood urea was 38 mg. for each 100 cc. Cystoscopic examination showed the function of both kidneys to be slightly reduced and equal. The clinical diagnosis was bilateral nephrolithiasis with



Fig. 3 (case 4).—Stone in the ureter, extra-ureteral stones, and multiple stones in the area of the left kidney.

large branched stones filling the pelvis of the kidneys, stone in the bladder, and moderate renal insufficiency. A stone 4 by 3 cm. was removed from the bladder by litholapaxy.

Comment.—The destruction of renal tissue and the possibility of renal fistulas resulting from the removal of multiple renal stones of this type contraindicate surgical procedure unless the symptoms are so severe that life is practically unbearable. Fortunately, it is rare that large coralliform stones are the cause of acute symptoms; occasionally

Comment.—In case of multiple stones in the kidney and ureter, and destruction of renal function, combined nephro-ureterectomy is advisable. The patient's condition may occasionally make it advisable to perform nephrectomy first and ureterolithotomy later. Large multiple stones in the ureter, if not removed, may cause considerable local infection. A widely dilated and infected ureter may act as a pocket of infection and should also be removed. If the stone is single and not larger than 1 cm., it can usually be left in situ for the time being. The majority of such stones will not cause further trouble, but should be removed if pocketing of regurgitated urine develops. Shadows of multiple stones in the left kidney and lower portion of the left ureter may be seen in figure 2.

CASE 4.—*Multiple stones in one kidney and stone in the lower portion of the ureter on the other side.*

A man, aged 32, had had repeated attacks of pain in the right lumbar area with anterior radiation during the last two years. The results of a general examination were negative. Urinalysis disclosed 50 pus cells to a field. Roentgenograms contained shadows suggestive of stone in the area of the right portion of the ureter, 1.5 by 1 cm. in diameter, probable phleboliths and shadows of multiple stones in the left kidney, the larger 2 by 2 cm. in diameter. On cystoscopic examination, the urine from both ureteral orifices was clear, and the function of both kidneys was equal and almost normal. An unsuccessful attempt was made to remove the stone from the right ureter by manipulation. At operation, right ureterolithotomy was first performed and two weeks later left pelvolithotomy.

Comment.—With stone in the ureter on one side and multiple stones in the kidney on the other side, as in this case, the indications for surgical intervention are the same as in cases of bilateral nephrolithiasis; in other words, the side which presents the most acute recent symptoms should usually be operated on first. In this case, the indication was to remove the stone in the right ureter first. Its removal by means of cystoscopic manipulation might be tried, but because of the danger of subsequent pyelonephritis and because of multiple stones in the kidney on the other side, only one or two attempts should be made. The possibility of one of the stones in the left kidney becoming displaced and obstructing the ureter with resulting anuria must always be considered. If, therefore, the acute symptoms were caused by the renal stone, nephrolithotomy should be performed first, and later manipulation of the stone in the other ureter. In figure 3, the shadow of the ureteral stone is included in the outline of the ureter which, together with the pelvis, is moderately dilated. The other shadows are shown to be extra-ureteral. Shadows of multiple stones are visible in the area of the left kidney.

Comment.—In case of multiple small stones in the renal pelvis, there should not be any unnecessary delay in operating because of the danger that one of the stones may pass into the lower portion of the ureter. In such a case, if the stone cannot be removed easily by manipulation, the extra operation is indicated. It is remarkable how often the smaller renal stones will pass into the ureter while the patient is under observation, apparently influenced by the purging and manipulation incident to roentgenography and cystoscopy. Manipulation of a



Fig. 5 (case 6).—The stone over the twelfth rib on the right side moved into the lower portion of the ureter.

stone in the lower portion of the ureter in the presence of multiple stones in the kidney is more likely to be followed by acute renal infection than in uncomplicated cases. In figure 5 the smaller stone shadow, which appeared over the twelfth rib on the right side, has now moved into the lower portion of the ureter.

CASE 7.—Bilateral nephrolithiasis: age as a factor in determining operation.

A rather feeble man, aged 68, had had dull pain in the left lumbar area at intervals for four years. He had also experienced similar pain in the right flank on several occasions during the last year. Results of physical examination were

a fragment breaks off and obstructs the ureter. Ureterolithotomy or cystoscopic manipulation should then be performed in selected cases. The shadows of multiple branched stones, filling the pelvis and calices of both kidneys, and of the stone in the bladder are shown in figure 4.

CASE 6.—*Bilateral stones, multiple in one kidney with single stone in the other.*

A man, aged 43, gave a history of repeated attacks of colic in the areas of both kidneys, more recently on the right side. Results of physical examination were negative, except for slight tenderness over the right kidney. Urinalysis-

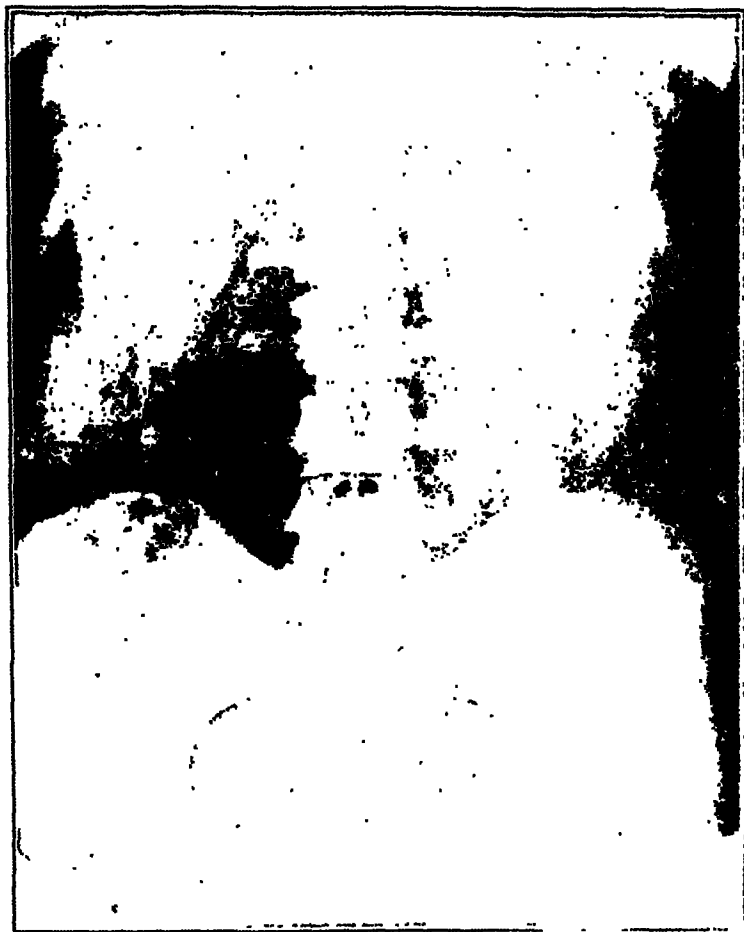


Fig. 4 (case 5).—Multiple branched stones filling the pelvis and calices of both kidneys, and stone in the bladder.

showed 32 pus cells to a field. The output of phenolsulphonphthalein was 20 per cent in two hours and the blood urea was 64 mg. for each 100 cc. Roentgenograms showed one large and one small shadow in the area of the right kidney and a single medium-sized shadow in the area of the left kidney. While the patient was being observed and a cystoscopy performed, the smaller stone passed from the right kidney to the lower portion of the ureter. It was necessary to perform a right ureterolithotomy at once. A right pelvolithotomy was performed several weeks later.

cal examination revealed tenderness over both kidneys. The two hour output of phenolsulphonphthalein was 45 per cent. Roentgenograms showed a huge, branched stone and multiple smaller stones in the area of the left kidney and two stones, 1.5 by 1 cm. in diameter, in the area of the right kidney. The outline of the right kidney in the roentgenogram apparently indicates hypertrophy. Cystoscopic examination showed normal function of the right kidney and only slight function in the left. Right pelviolithotomy was performed, followed by left nephrectomy.

Comment.—In cases of bilateral stones of this type, in the absence of recent acute symptoms, it is usually advisable to operate first on the



Fig. 7 (case 8).—Huge branched stone and multiple small stones in the area of the left kidney, and two small stones in the area of the right kidney.

kidney that functions better so as to take advantage of the remaining function of the other kidney. After the function of the better kidney has returned to normal, the other kidney can be more safely removed. In this case, immediate right pelviolithotomy was indicated, even though the size of the stone was favorable for spontaneous passage. Under the circumstances, the danger of ureteral obstruction by a migrating ureteral stone is obvious. In figure 7 the shadows of a huge branched stone and multiple small stones appear in the area of the left kidney, and the shadows of two small stones in the area of the right kidney.

negative. Urinalysis showed 60 pus cells to a field. The two hour phenolsulphonphthalein output was 30 per cent, and the blood urea was 58 mg. for each 100 cc. Roentgenograms revealed bilateral nephrolithiasis and multiple round stones in both kidneys. In the left kidney, the largest shadow was 3 by 4 cm., with many small shadows. In the right kidney, the largest shadow was 2 by 3 cm.; there were multiple smaller shadows. Cystoscopic examination demonstrated that the comparative function of the two kidneys was greatly reduced, that of the left kidney being somewhat better than that of the right. It was thought inadvisable to operate on this patient because of lack of acute symptoms and also because of his age.



Fig. 6 (case 7).—Multiple bilateral renal stones.

Comment.—If the patient had been 20 or 30 years younger, operation might have been indicated, since his vitality and the life expectancy might then have justified the risk. The shape of the stones might have permitted operation. The comparatively round or smooth stones, even though multiple, would not have necessitated much destruction of tissue. Figure 6 shows shadows of multiple, bilateral renal stones.

CASE 8.—*Bilateral nephrolithiasis with one kidney practically normal and the other normal*

A man, aged 25, had had attacks of severe pain in both kidneys since the age of 7 years. Recently the pain had been referred entirely to the right side. The

kidney with the better function first, and, if indicated, to remove the other kidney later. Since the pain in this case was practically the same on both sides, it was deemed advisable to operate on the right kidney first because of its better function, and to remove the stone in the ureter before pelviolithotomy was attempted. As the stones were not branched and, therefore, were not wedged into the calices, they could be removed without much injury to the renal tissue. The indefinite hazy shadow adjacent to the shadows of the larger stones is explained by sandy material. Even though this is not completely removed, there is seldom danger that it will act as a nucleus for the formation of other stones if adequate drainage is established. In figure 8 may be seen the shadows of multiple stones in the areas of both kidneys. The stone in the lower portion of the left ureter is not visible in the roentgenogram.

CASE 10.—Bilateral nephrolithiasis: multiple small stones in one kidney and a single small stone in the other.

A woman, aged 32, gave a history of intermittent colic referred to the right loin, accompanied by pyuria, and chills and fever during a period of two and a half years. Several small stones had passed during these attacks. There were no symptoms referable to the left kidney. The results of a general physical examination were negative. The roentgenograms contained multiple scattered shadows of stones varying in size from 0.5 to 1 cm. in the area of the right kidney, and the shadow of a single stone 1 cm. in diameter in the area of the left kidney. On cystoscopic examination, the function of both kidneys was found to be normal and equal, and by means of urography the shadows were shown to be intrarenal. A diagnosis was made of bilateral nephrolithiasis, multiple small stones in the right kidney and a single stone in the left kidney. Combined nephropelviolithotomy was performed, and five cortical stones were removed from the right kidney. Fluoroscopic examination on the operating table showed that the kidney was free from stones. This observation was corroborated by a postoperative roentgenogram. The stone from the left kidney passed after an attack of colic. Cystoscopic examination one month later showed the function of both kidneys to be normal.

Comment.—It was thought advisable in this case to remove the stones from the right kidney only because the stone in the left was single, was not causing acute symptoms and was small enough to pass. The removal of multiple small stones scattered widely in the kidney may be exceedingly difficult, but with the aid of renal fluoroscopy their complete removal with a minimum of renal injury is usually possible. In figure 9 are seen the shadows of multiple small stones in the right kidney and a small single stone in the left kidney.

CASE 11.—Multiple, bilateral stones with conservative operation indicated for both kidneys.

A man, aged 48, gave a history of having passed stones and sand at intervals since he was 8 months old. Pain was always confined to the left side of the abdomen and had been more acute recently. The urine had been cloudy for years. The results of the physical examination were negative except that acute tender-

CASE 9.—Operable bilateral nephrolithiasis, together with stone in the ureter.

A woman, aged 47, came to the clinic with a history of repeated attacks of colic referable to the left renal area and occasional dull pain in the right. The results of a general physical examination were negative. The roentgenograms showed shadows of multiple stones in the area of the right kidney, and one or more in the area of the left kidney, as well as a shadow 2 mm. in diameter in the area of the lower portion of the left ureter. Cystoscopic examination showed the function of both kidneys to be somewhat less than normal, the function of the right being slightly better than that of the left. A stone was seen partially protruding from the left ureteral orifice: this was cut, and it subsequently passed.



Fig. 8 (case 9).—Multiple stones in the areas of both kidneys.

Right pelviolithotomy was performed and a single staghorn stone was removed from the kidney, together with much sandy material. Subsequently, a left pelviolithotomy was done, and a stone, 2 by 2 cm. in diameter, a number of small stones and some sandy material were removed. Two months after operation the function of both kidneys was normal and equal. Subsequent roentgenograms were negative.

Comment.—In the presence of bilateral nephrolithiasis, it is usually advisable to operate first on the kidney causing recent acute symptoms. If the symptoms are not acute, it is usually advisable to operate on the

stone remain in the left kidney, but they are in the ends of the calices, where they will probably cause little further injury. Should they increase in size, they can be more easily found and removed later. The fact that twelve stones were removed from the right kidney and that a postoperative roentgenogram was negative attest to the value of fluoroscopy. Postoperative cystoscopy showed marked improvement in the function of both kidneys. The possibility for improvement in renal function following operation for multiple stones is greater when localized areas of infection are present than when they are not.



Fig. 10 (case 12).—Two large stones in both lower ureteral areas, with lead catheters adjacent to them.

CASE 12.—Bilateral large ureteral stones.

A man, aged 28, had had dull pain, referred to the areas of both kidneys, pyuria and intermittent spells of fever for many years. Physical examination revealed cachexia and severe anemia. Urinalysis showed a large amount of pus. The phenolsulphonphthalein return in two hours was 15 per cent, and the blood urea 44 mg. for each 100 cc. Roentgenograms showed two large shadows in the area of the bladder, which might have been caused by stones in the diverticula of the bladder or in the ureters. On cystoscopic examination, multiple diverticula

ness was evident over the left lumbar area. Urinalysis revealed pus in large quantities. The two hour output of phenolsulphonphthalein was 15 per cent.; and the blood urea was 52 mg. for each 100 cc. Roentgenograms showed multiple shadows scattered over the areas of both kidneys. On cystoscopic examination, the urine from both kidneys was found to be cloudy, and the function of both kidneys to be greatly and equally reduced. A diagnosis was made of multiple stones in both kidneys with reduced function and infection. Eight stones were removed from the left kidney by combined nephropelviolithotomy. The kidney was three times the normal size and contained a great deal of pus. Although



Fig. 9 (case 10).—Multiple stones in the right kidney and a single stone in the left kidney.

fluoroscopic examination showed two remaining shadows, it was considered advisable not to carry on the search since the patient was weak and the removal of the stones would have necessitated much destruction of renal tissue. Subsequently a right nephropelviolithotomy was performed and twelve stones were removed. Postoperative roentgenograms showed two fragments of stone remaining in the left renal area and none in the right.

Comment.—The case illustrates the extent to which conservative operation can be successfully carried out in bilateral multiple nephrolithiasis by employing renal fluoroscopy. It is true that two fragments of

the upper portion of the ureter and pelvis. An attempt should be made to find the smaller stones first, since the larger stones can be picked up readily. Fortunately, in this case the stones passed following cystoscopic manipulation, although their presence caused a ureteral fistula for a period of several weeks.

CASE 14.—Stone in kidney, ureter and bladder.

A man, aged 38, was examined at the Clinic in February, 1925. Five years previously, he had had an attack of sharp colic referred to the upper right quadrant of the abdomen and to the lumbar area, which required several hypodermic injections for relief. Since then he had had similar attacks of pain at intervals of from two to six months. Three years previously, a stone, about 0.5 by 1 cm., had passed with hematuria. One week before he came to the clinic, the pain had been referred to the left kidney, with anuria for two days. A roentgenogram made elsewhere showed the shadows of stones in both kidneys. Recently he had complained of anuria and nausea, but he was otherwise normal. Urinalysis showed the presence of a moderate number of pus cells and red blood cells. The roentgenograms contained what appeared to be shadows of stones in the bladder, right ureter and right kidney. There was no trace of phenolsulphonphthalein in two hours; the blood urea was 282 mg. for each 100 cc., and blood creatinine was 7. A low protein diet, hot packs and forced fluids were prescribed. In three days, the blood urea dropped to 112 and the creatinine to 4.8. The diet was continued, and a week later the blood urea was 36 and the phenolsulphonphthalein return 30 per cent. On cystoscopic examination, a diagnosis was made of stone in the bladder, 2 by 1.5 cm., which had apparently recently passed from the left kidney; this explained the rapid drop in the blood urea. A urogram localized a shadow in the middle third of the right ureter, and the shadow in the kidney was included in the outline of the renal pelvis. The function of the right kidney was moderately reduced. The stone was removed from the bladder by litholapaxy. Through a right posterolateral incision, the ureteral stone situated at the middle portion of the ureter was worked back into the pelvis and removed, together with the stones in the kidney.

Comment.—The fact of greatest interest in this case was the evidence of marked renal insufficiency. In cases of multiple renal stones, the question not infrequently arises, whether operation is indicated in the presence of high blood urea retention. If there is acute ureteral obstruction, immediate operation would, of course, be advisable. In the absence of such obstruction, unless evidence of renal insufficiency can be materially eliminated by placing the patient in the hospital and prescribing a low protein diet, forced fluids and elimination, the advisability of operation is questionable. The anuria and evidence of retained nitrogenous elements in this case can be explained by the recent blockage of the left kidney by the ureteral stone, now in the bladder, and the presence of multiple stones in the right kidney and ureter. It is interesting to note the limits that the urea can attain as a result of urinary retention and then return to normal following reestablishment of urinary drainage and other treatment. In the presence of coincident stone in the bladder and kidney, litholapaxy is usually indicated, and it saves the

were found, but stones were not visible. A cystogram showed the outline of the stones extending beyond the outline of the bladder, so that it was evident that they were intra-ureteral. This was further corroborated by lead catheters introduced into the ureters, which were found in a urogram to be adjacent to and partially coiled around the stone. A diagnosis of two large bilateral ureteral stones and multiple diverticula of the bladder was made. At the operation, bilateral ureterolithotomy was performed, the right side being operated on first. Later the diverticula were resected.

Comment.—It is evident that any attempt at manipulation of stones of this size in a ureter is contraindicated. When complicated by diverticula in the bladder, as in this case, they should be removed before the latter are resected, because of the possibility of ureteral obstruction. Furthermore, renal function should be as nearly normal as possible before major operation on the bladder is attempted. In figure 10 the outline of two large stones is visible in both lower ureteral areas, with lead ureteral catheters adjacent to them.

CASE 13.—Multiple stones in ureter; difficulties in removal.

A man, aged 53, presented himself for examination in April, 1924. In 1915, a stone had been removed elsewhere from the right ureter. In 1916, three small calculi passed while the patient had colic referred to the area of the left kidney. Six months previous to the time he was examined, he experienced severe colic in the left side, and at that time roentgenograms showed a shadow opposite the third lumbar vertebra and a smaller one in the kidney. Since then a dull, dragging feeling had been noted in the left flank in the morning. Roentgenograms showed a shadow under the fourth transverse process on the left side, apparently due to multiple calculi. Urinalysis showed the presence of a few microscopic pus cells, and tests of renal function were negative. On cystoscopic examination, an impassable obstruction was met by the catheter 15 cm. above the ureteral orifice. A ureterogram showed slight dilatation of the left lower third of the ureter. There was no evidence of iodide above the shadow of the larger stone. A diagnosis was made of multiple stones in the lower third of the ureter, the largest being 2 by 2 cm., with two smaller stones just above it.

Ureterolithotomy was performed, and only one stone corresponding in size to the larger shadow could be found. The ureter was dilated above this, and it was thought possible that the smaller stones might have passed up into the kidney. A persisting fistula remained in the ureter for several weeks following the operation. Postoperative roentgenograms showed two small stones in the lower third portion of the left ureter. Several ureteral catheters were introduced into the ureter full length and fastened in it. Following repeated manipulations, both stones passed.

Comment.—With multiple stones in the ureter, and particularly if the lower one is the larger and impacted, it is logical to assume that the ureter above is greatly dilated. In such cases extra precautions should be taken not to permit the smaller stones to escape from the field of operation. With the relaxation caused by anesthesia and with the patient in the Trendelenburg position, even though the proximal portion of the ureter is partially clamped, a small stone may escape into

never had any urinary symptoms. The results of a general examination were negative, including tests of renal function. Urinalysis disclosed an occasional pus cell. A renal roentgenogram contained two shadows apparently in the area of the left kidney, the larger being 1 by 1 cm. On cystoscopic examination and pyelography, an anomalous pelvis of a fused left kidney was found. The original shadows of the stones were included in the outline of the pelvis. Anomalous lateral insertion of the ureter with evidence of abnormal rotation of the pelvis was typical of a fused kidney. A subsequent pyelogram of the right side showed a similar condition. The function of both kidneys was practically normal. A diagnosis was made of multiple stones in the left pelvis of a fused kidney.

The fused kidney was revealed through an anterior incision. The pelvis of the left half of the kidney was extremely dilated, and a stone, 1.5 by 1.75 cm., was removed. The stone was shaped like a dumb-bell, giving the appearance of a second stone in the preoperative roentgenogram. Other stones could not be found on exploration.

Comment.—Multiple stones in a fused kidney offer peculiar complications in judging the necessity of surgical intervention. If the stones are large and branched, filling the pelvis of the kidney, without causing significant symptoms, an operation is hardly indicated. It must be admitted that the difficulties of operation in a fused kidney are greater than in the normal kidney. As a rule, the anterior approach with conservative operation in a fused kidney is preferable to the posterior incision. The difficulty in delivering the kidney and in completely removing the stone is necessarily greater. Unless the patient is unusually thin, it is impossible to employ renal fluoroscopy in the presence of a fused kidney, and the use of roentgen-ray films on the operating table might be applicable.

Stones shaped like dumb-bells frequently give the appearance of multiple stones. One must be certain, however, that another stone is not present, even though the shape of the stone is such that it could cast two shadows. The position of a stone of this type in itself would be suggestive of renal anomaly, since multiple stones of this kind usually are not present in the ureter. In a fused kidney, they are generally near the median line, as in this case. The appearance of the pyelogram, and particularly the insertion of the ureter and the rotation of the calices, are typical of horseshoe kidney, and it should be easily recognized.

In figure 11 the pelvis of the left kidney is visible, with two original shadows obscured by the pelvis, which is slightly dilated. Failure of complete rotation of the pelvis is typical of fused kidney. The calices are dilated.

patient from undergoing an operation. Under such circumstances, the stone in the bladder is usually of renal origin. Also of interest in this case was the ability to work the stone in the ureter up into the pelvis so that it could be removed together with the renal stone through one incision. This, of course, is possible only when the stone is not too large and irregular and when the ureter is large enough to permit it. As seen in the urogram, the ureter was hardly large enough to permit this, but it was probably not completely distended. The pelvis and



Fig. 11 (case 15).—Two original shadows obscured by the pelvis of the left kidney.

calices may be normal in spite of the presence of a stone in the kidney and ureter.

CASE 15.—Stones in the left half of a fused kidney.

A man, aged 39, presented himself for examination at the clinic in July, 1924. His gallbladder and appendix had been removed at another hospital in 1921. Eight months prior to examination, he first noticed sharp pain originating in the lower left abdominal quadrant and radiating through to the back and downward into the area of the bladder. Four severe attacks during the last three months before he came to the clinic had required the administration of morphine. He had

never had any urinary symptoms. The results of a general examination were negative, including tests of renal function. Urinalysis disclosed an occasional pus cell. A renal roentgenogram contained two shadows apparently in the area of the left kidney, the larger being 1 by 1 cm. On cystoscopic examination and pyelography, an anomalous pelvis of a fused left kidney was found. The original shadows of the stones were included in the outline of the pelvis. Anomalous lateral insertion of the ureter with evidence of abnormal rotation of the pelvis was typical of a fused kidney. A subsequent pyelogram of the right side showed a similar condition. The function of both kidneys was practically normal. A diagnosis was made of multiple stones in the left pelvis of a fused kidney.

The fused kidney was revealed through an anterior incision. The pelvis of the left half of the kidney was extremely dilated, and a stone, 1.5 by 1.75 cm., was removed. The stone was shaped like a dumb-bell, giving the appearance of a second stone in the preoperative roentgenogram. Other stones could not be found on exploration.

Comment.—Multiple stones in a fused kidney offer peculiar complications in judging the necessity of surgical intervention. If the stones are large and branched, filling the pelvis of the kidney, without causing significant symptoms, an operation is hardly indicated. It must be admitted that the difficulties of operation in a fused kidney are greater than in the normal kidney. As a rule, the anterior approach with conservative operation in a fused kidney is preferable to the posterior incision. The difficulty in delivering the kidney and in completely removing the stone is necessarily greater. Unless the patient is unusually thin, it is impossible to employ renal fluoroscopy in the presence of a fused kidney, and the use of roentgen-ray films on the operating table might be applicable.

Stones shaped like dumb-bells frequently give the appearance of multiple stones. One must be certain, however, that another stone is not present, even though the shape of the stone is such that it could cast two shadows. The position of a stone of this type in itself would be suggestive of renal anomaly, since multiple stones of this kind usually are not present in the ureter. In a fused kidney, they are generally near the median line, as in this case. The appearance of the pyelogram, and particularly the insertion of the ureter and the rotation of the calices, are typical of horseshoe kidney, and it should be easily recognized.

In figure 11 the pelvis of the left kidney is visible, with two original shadows obscured by the pelvis, which is slightly dilated. Failure of complete rotation of the pelvis is typical of fused kidney. The calices are dilated.

others have emphasized the importance of the pylorus in relation to chronic ulcer in man. In Fenwick's⁷ statistics from human beings 75 per cent of the chronic gastric ulcers occur in this region, while, experimentally, acute lesions frequently show a delay in healing in the pylorus. More trauma is produced in this area from food and gastric juice than in other areas of the stomach (Friedman and Hamburger,⁸ Morton⁹ and others).

Konjetzny¹⁰ discussed the importance of injury to the mucosa from food and reported some interesting observations on weaned calves. Gastritis, multiple erosions and chronic ulcers were found in the stomach after the diet was changed from milk to rough food. These lesions healed when the calves were again put on a milk diet. He concluded that trauma was most important and that the gastric juice was of minor importance in the etiology of these lesions. Baggio¹¹ also produced chronic gastric ulcer experimentally when he fed a coarse diet mixed with 3 per cent hydrochloric acid, but he failed to produce ulcers when he fed acid alone. His experiments, however, are too few to permit of any definite conclusions.

Many types of operations have been performed for the purpose of studying the influence of acid on ulcers, by increasing the secretion of acid or prevention of neutralization by deflection of the duodenal contents into the ileum. Other methods have been the injection of quantities of acid into the stomach. Matthes,¹² in 1893, used this method in one dog and produced a delay in the healing of an acute ulcer. In investigations on monkeys and cats, Bolton¹³ made a more extensive study of this method of artificial hyperacidity. He fed the animals acid solutions varying from 0.18 to 1.5 per cent. He concluded that the destructive power of gastric juice was due to the hydrochloric acid present and that the acid was usually a factor in the initiation of an ulcer.

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EFFECTS OF INJECTIONS OF ACID AND TRAUMA ON JEJUNAL TRANSPLANTS TO THE STOMACH

WILLIAM J. GALLAGHER, M.D.

Seymour Coman Fellow in the Department of Physiology of the University of
Chicago and the Department of Surgery of Rush Medical College
of the University of Chicago

CHICAGO

Experimental data are presented on further studies on intestinal segments transplanted to the stomach. Particular study has been made of the influences of the chemical and traumatic factors in the etiology of ulcer.

The almost constant observation of hydrochloric acid in clinical peptic ulcer has frequently led to the conclusion that it is an essential element in its production. Experimentally, however, it has been rather definitely established by many workers that uninjured intestinal mucosa is unaffected by exposure to the digestive action of gastric juice.

Isolated segments of intestine, with their blood supply intact, transplanted to the stomachs of dogs, remained unchanged in the experiments of Hotz¹ and Licini.² Later, Dragstedt and Vaughn³ showed that various parts of the intestinal tract, kidney and spleen transplanted to the stomach remained normal when subjected to the digestive action of gastric juice for long periods. In an experimental study of transplants to different areas of the stomach, De Takats and Mann⁴ obtained a small percentage of chronic ulcers in patches on the lesser curvature of the stomach near the pylorus. The percentage of chronic ulcers was even greater, when a surgical duodenal drainage was also performed (Morton⁵). The acid-alkali imbalance produced in the stomach by the latter operation and the mechanical stress to the patch on the lesser curvature were the causative factors in these ulcers. Aschoff⁶ and

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EXPERIMENTAL METHODS

Normal, healthy dogs were used. All operations were done aseptically under ether and morphine anesthesia. After recovery from the operation, the animals were given a diet of meat, bones, bread and water. The nutritional condition remained good in most of the animals until ulcers developed. The acid solutions had a tendency to decrease the animal's appetite, particularly those of a higher concentration. Variations in the amount and frequency of the injection of acid usually obviated this condition.

Openings about 8 by 4 cm. were made in different areas of the anterior or posterior walls of the stomach. Many of these openings were made close to the lesser and greater curvatures and about 4 cm. from the pyloric sphincter. A suitable length about 8 to 13 cm. of a freely movable part of the jejunum, with its blood supply maintained, was sutured into the selected areas of the stomach. The ends of the isolated segment were closed by catgut pursestring sutures. The continuity of the bowel was reestablished by end to end anastomosis, and in several by lateral anastomosis. The segment formed a part of the stomach wall with pouching of the pursestringed ends into which gastric juice and food would gravitate.

In three animals, after healing was complete, 0.62 per cent acid barium solution was injected; roentgenograms were then taken to determine the condition and position of the transplant and its effect on the emptying time of the stomach.

Exploratory operations were performed at various times from 12 to 112 days after transplantation. In five of the animals acute traumatic lesions of the transplant mucosa were made in various locations. Young's clamps were applied in one or two areas for from thirty-five to fifty minutes to produce these lesions. (In previous experiments¹⁴ these pressures were found to produce acute penetrating ulcers of the duodenum jejunum.) In a group of seven animals, five of which had traumatic lesions, injections of hydrochloric acid were started two days after the production of the lesion of the transplant mucosa. The injections of acid were given through an Ewald stomach tube without an anesthetic for from twenty-four to fifty-eight days. In some instances the acid solution was given twice daily in amounts of from 200 to 225 cc. The concentrations of the solution were 0.22, 0.29 and 0.62 per cent. The percentages were obtained by using 3, 3.5 and 9 cc., respectively, of a 35 per cent hydrochloric acid added to sufficient water to make 550 cc. (these solutions were titrated with decinormal sodium hydroxide and found to agree with the foregoing percentages). If the solutions were injected too rapidly or in quantities of more than 225 cc., vomiting would occur immediately. This was especially true with the higher percentage of acid solution. Aspirations of the stomach from four to five hours after injection frequently gave negative results except in those animals in which a retention had been present.

Results.—Twenty-four animals with jejunal transplants were studied for a period of from 12 to 154 days. Several animals that developed an intussusception of the lateral anastomosis were not included in the group. Chronic intussusception was found in four of the group, resulting in some emaciation, but the transplant remained normal.

Seventeen animals were used for control study. Chronic ulcers occurred on the proximal and distal ends of the transplant in two, fifty-four and sixty-nine

14. Gallagher, W. J.: Acute Traumatic Ulcer of Small Intestine. *Arch. Surg.* 15:689 (Nov.) 1927.

TABLE 1.—*A Series of Jejunal Loop Transplants to Stomach*

| Ex- peri- ment | Date of Opera- tion | Location of Transplant | Exploratory Operation | Interval, Days | Remarks |
|----------------------|---------------------------|---|---|-------------------|---|
| 1 | 2/25/27 | Posterior wall near greater curvature | Intestinal obstruc- tion at site of anastomosis | 151 | Normal transplant mucosa; dilatation of duodenum |
| 2 | 3/ 9/27 | Middle of ante- rior wall | Intussusception of intestinal anas- tomosis | 48 | Transplant normal |
| 3 | 4/10/27 | Posterior wall near lesser curvature | Intussusception of lateral anas- tomosis | 62 | Emaciation, normal trans- plant mucosa |
| 4 | 4/10/27 | Middle of pos- terior wall | Transplant healed | 12 | Distemper developed |
| 5 | 4/ 8/27 | Posterior wall near greater curvature | Two chronic ulcers on ends of trans- plant 1.2 by 1 and 0.3 by 0.3 cm. | 69 | Much scar tissue at base of distal ulcer |
| 6 | 4/ 9/27 | Posterior wall near lesser curvature | Normal transplant mucosa | 58 | Marked narrowing of end to end anastomosis; some ema- ciation |
| 7 | 4/30/27 | Anterior wall, lesser curva- ture near pylorus | Normal transplant mucosa | 72 | Some emaciation |
| 8 | 4/22/27 | Anterior wall, midportion | Chronic ulcer on distal end of transplant 1 by 1 cm. | 51 | Some emaciation present |
| 9 | 4/23/27 | Middle of an- terior wall | Normal transplant mucosa | 44 | Developed distemper |
| 10 | 4/23/27 | Anterior wall near greater curvature | Sharp spicule of bone perforating distal end of transplant | 33 | Serofanguinous exudate in peri- toneal cavity; normal trans- plant mucosa |
| 11 | 5/ 5/27 | Anterior wall near lesser curvature | Normal transplant mucosa | 45 | Obstruction of duodenum due to hair ball |
| 12 | 7/12/27 | Middle of pos- terior wall | Normal mucosa | 26 | Some emaciation |
| 13 | 7/ 2/27 | Anterior wall near lesser curvature | Normal mucosa | 36 | Developed di-temper |
| 14 | 6/14/27 | Middle of an- terior wall | Normal mucosa | 21 | Developed distemper |
| 15 | 7/16/27 | Anterior wall near lesser curvature | Normal mucosa | 22 | Death from anesthesia during exploratory operation |
| 16 | 7/18/27 | Anterior wall near lesser curvature | Spicule of bone per- forating distal loop transplant; perforation closed by pursestring suture | 42 | Animal died one month after exploratory operation; nor- mal mucosa |
| 17 | 8/ 1/27 | Anterior wall near greater curvature | Normal mucosa | 14 | Condition poor after operation; loss of appetite; died |

and 0.6 by 0.3 cm., were found in one animal of the seven, on the proximal and distal ends of the transplant, on the fifty-sixth day of the injections of acid and the one hundred and sixteenth day after operation. The mucosa of the transplant of this animal between the ends was hyperemic, slightly swollen and covered with mucus. This transplant was located on the posterior wall about 2 cm. from the greater curvature, near the pylorus. Edema, some hyperemia and a few petechiae



Fig. 2.—Jejunal loop with chronic ulcers on ends found sixty-nine days after transplantation to posterior wall of the stomach; lateral anastomosis of intestine, containing a fragment of bone in the free end.

were present in the mucosa of four of the animals in the group in which injections of acid were given. An appreciable amount of tenacious mucus was a constant observation in the stomachs and transplants of animals that received acid solutions. Larger amounts were found after the injection of the 0.62 per cent solution than after the use of 0.22 or 0.29 per cent acid. All the acute lesions

days after operation. These transplants were on the posterior and anterior wall of the stomach near the greater curvature. The mucosa was otherwise normal in these as well as the remaining seventeen control experiments. Microscopically, a moderate amount of scar tissue was present in the healed ends of the transplant. There was a marked tendency to pouch formation of the transplant. In a few of the animals, there was a dilatation of the stomach and transplant with a



Fig. 1.—Photograph taken after fixation of stomach in formaldehyde. Stomach and jejunal loop greatly dilated; loop in stomach 151 days; injections of 0.22 acid solution were made daily for 33 days; ulcers were not observed.

tendency to retention. A sharp spicule of bone was found in the distal end of the transplant in two animals. One of the spicules had perforated the transplant with a resulting serosanguinous exudate in the peritoneal cavity. A chronic ulcer, mentioned previously, was found on the end of the transplant of the other animal. In the group in which injections of acid were made, two chronic ulcers, 0.5 by 0.2

Effects of Hydrochloric Acid Into Stomachs with Jejunal Transplants (Acute Reduced by Clamp Pressure)

| Experiment | Date of Operation | Location of Transplant | Injection of Hydrochloric Acid | | Acute Traumatic Lesion | | Interval, Days | Necropsy Results | Remarks |
|------------|-------------------|--|-----------------------------------|--------------------|------------------------|------------------------|----------------|--|---|
| | | | Per-centage injected, Cc. of Days | Amount In-Number | Date of Operation | Location of Transplant | | | |
| 18 | 2/12/27 | Posterior wall, middle | 0.52 | 200 | 33 | 5/11/27 | 151 | Dilated stomach, much mucus present; hyperemia of transplanted lesion healed | Edema of lungs from aspiration of acid solution |
| 19 | 4/13/27 | Posterior wall, near greater curvature | 0.29 | 200 | 50 | | 110 | Edema of transplant mucosa; two chronic ulcers on ends of transplant, 0.5 by 0.2 and 0.6 by 0.3 cm.; mucus in stomach by 0.3 cm.; mucus in stomach and petechiae of transplant; mucus in stomach and traumatic lesion healed | Frequent vomiting of mucus and acid solution |
| 20 | 4/15/27 | Middle of posterior wall | 0.29 0.02 | 200 twice daily | 53 20 | 8/ 5/27 | 154 | Edema and petechiae of transplant mucosa; mucus in stomach and traumatic lesion healed | Developed symptoms of acidosis |
| 21 | 6/11/27 | Middle of anterior wall | 0.22 | 200 | 32 | | 78 | Mucus in stomach normal | Frequent vomiting of acid solution |
| 22 | 7/10/27 | Posterior wall near lesser curvature | 0.02 | 200 | 60 | 8/10/27 | 73 | Traumatic lesion healed; much mucus present; some edema of transplant mucosa | Slight cellular exudate in mucosa of transplant |
| 23 | 7/27/27 | Anterior wall near greater curvature | 0.02 0.02 | 200 twice daily | 27 32 | 8/ 8/27 | 41 | Healed traumatic lesion; some edema of transplant mucosa; much mucus present | Developed symptoms of acidosis |
| 24 | 8/ 2/27 | Anterior wall near lesser curvature | 0.12 0.02 | 200 twice daily | .. | 8/10/27 | 41 | Edema and petechiae of mucosa present; traumatic lesion healed; much mucus present in stomach and transplant | Slight cellular exudate in mucosa of transplant; developed symptoms of acidosis |

produced by clamps had completely healed leaving little evidence grossly of scar formation. After injection of acid for from three to four weeks, some of the animals developed symptoms of acidosis.

Microscopically, there was a moderate amount of cellular exudate in the mucosa of the transplant of the group which received injections of acid. Goblet cells were found in the mucosa of a few of the transplants.

COMMENT

Scar tissue was constantly present in the ends of the transplants, in which chronic ulcers were found in three animals. Consequently, the most important etiologic factor was undoubtedly the nutritional dis-



Fig. 3.—Photomicrograph of chronic ulcer on distal end of transplant shown in figure 2; superficial necrosis with abundant scar tissue in base of ulcer: $\times 32$.

turbance present in these regions of the transplant. The location of the segment in the stomach seemed to have little influence on the occurrence of ulcer in these experiments. In those transplants with chronic lesions, the distal lesion was always larger than the proximal one. This is logical, since the distal part was more frequently subjected to trauma from food and perhaps the action of gastric juice.

Several times at exploratory operation and postmortem examination, the distal end of the transplant contained food, bones and gastric juice, while the proximal end was usually empty. The tendency to retention in this portion of the transplant was also observed in the roentgen-ray

those in the control experiments, 112 days after operation and 58 days after the injection of 0.62 per cent hydrochloric acid. In four animals of this group, edema and some hyperemia of the mucosa were noted.

Gastric mucus was a constant observation in the stomachs and transplants of the series in which injections of acid were made. Acute traumatic ulcers of the transplants in six of the series with artificial hyperacidity healed with only slight gross changes. Nutritional disturbance of the ends of the transplants was suggested as the probable important factor to explain the presence of chronic ulcers found in these experiments. The gastric mucus and alkaline secretion of the intestine were considered an important protective influence to the mucosa against the irritant action of the hydrochloric acid solution injected.

CONCLUSION

In these experiments the attempt at artificial hyperacidity failed to increase the occurrence of chronic ulcer in the stomach itself, in the scar tissue of the transplant or in the transplant mucosa.

examination, when barium material was observed after the upper part of the transplant was empty. The tendency of the transplant to pouch formation protected the mucosa from the greater trauma from food and the action of gastric juice. It was also a factor in aiding the healing of acute traumatic lesions. Observations were not made on the time of healing of these lesions. Grossly and microscopically the healed lesions were not unlike those found in the duodenum and jejunum in previous experiments. Bolton¹³ reported a delayed healing of acute ulcers in the stomach following the injection of solutions of hydrochloric acid.

The constant presence of gastric mucus in the experiments with artificial hyperacidity was, no doubt, with the alkaline secretion of the intestine, a protective influence against the irritant action of the hydrochloric acid. Frequently vomiting of acid solutions, especially those of higher concentration, also decreased the efficiency of this method of hyperacidity. The rapid emptying of the stomach of acid solution (Carlson,¹⁵ Steinberg,¹⁶ Olch¹⁷ and others) still further limited the time of action of the acid on the transplant mucosa. The few changes observed (hyperemia and edema) are in part explained by these factors. The fact that the higher concentration of acid (0.62 per cent) did not produce any greater changes in the transplant mucosa than the lesser concentration solution (0.29 per cent) is further evidence of the protective influence of the various factors mentioned.

In these experiments, trauma, due to operation, and lessened blood supply to the ends of the transplant caused nutritional disturbances which determined the site of the mucosal ulceration.

SUMMARY

Chronic ulcers were observed on the ends of two transplants of seventeen animals, in which the blood supply to the loop was maintained. These transplants were on the posterior and anterior wall of the stomach near the greater curvature. The longest period of observation was 154 days.

An artificial hyperacidity was produced by injections of varying concentrations of hydrochloric acid from once to twice daily into the stomach in seven animals, for periods of from twenty-four to fifty-eight days. In one of these, two chronic ulcers were observed similar to

15. Carlson, A. J.: Personal communication to the author.

16. Steinberg, M. E.; Brougher, J. C., and Vidgoff, I. J.: Changes in the Chemistry of the Contents of the Stomach Following Gastric Operations, *Arch. Surg.* 15:749 (Nov.) 1927.

17. Olch, I. Y.: Duodenal Regurgitation as a Factor in Neutralization of Gastric Acidity, *Arch. Surg.* 16:125 (Jan.) 1928.

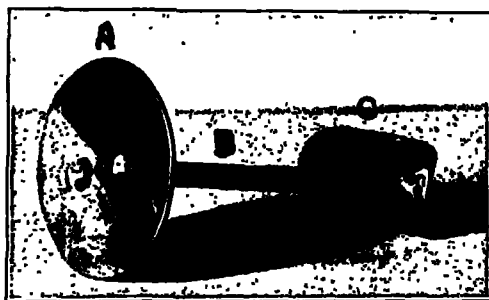


Fig. 2.—Depression in the plate (*A*) for the entrance of the needle into the tubes.



Fig 3.—Dog two weeks after operation. The arrow points to the instrument.

PHYSIOLOGY OF THE LIVER AND INTESTINE

METHOD OF STUDY *

CYRUS F. HORINE, M.D.

BALTIMORE

I shall make a preliminary report on a method for the study of the function of the intestine and liver, with particular reference to the study of the portal blood. This method is for experimental use in animals.

An instrument or permanent cannula is used between the portal vein and the skin of the abdominal wall. It is a gold plated cannula having two tubes.

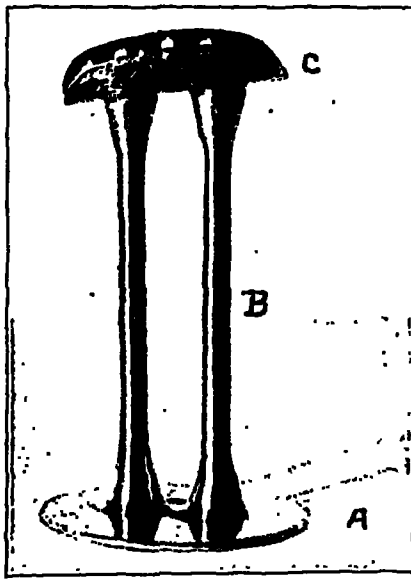


Fig. 1.—Instrument used in experiment.

These tubes barely allow the passage of an 18 gage record needle. Sterling silver tubing is used because it is impossible to plate the lumen of the tube.

The instrument consists of two tubes (*B*) connecting a concave portion (*C*) which is sutured over the portal vein to a round flat plate (*A*). The round flat plate is placed beneath the skin of the abdominal wall. It is about the size of a half silver dollar (fig. 1).

The operation is performed with the animal under general anesthesia. A half moon incision is made in the upper right quadrant. The convex surface of the incision points toward the midline. A longitudinal incision is made through the rectus muscle and peritoneum. The portal vein is exposed, and

* From the Department of Surgery, University of Maryland.

A great many dogs were killed because of infections in the wound. This was overcome by placing a silver wire drain (made of twisted strands of silver wire) in the wound, for a period of from two to three days. Otherwise the dogs would develop a collection of serum beneath the skin with a secondary infection of the wounds. The wounds usually heal in from ten days to two weeks, and the vein may then be aspirated.

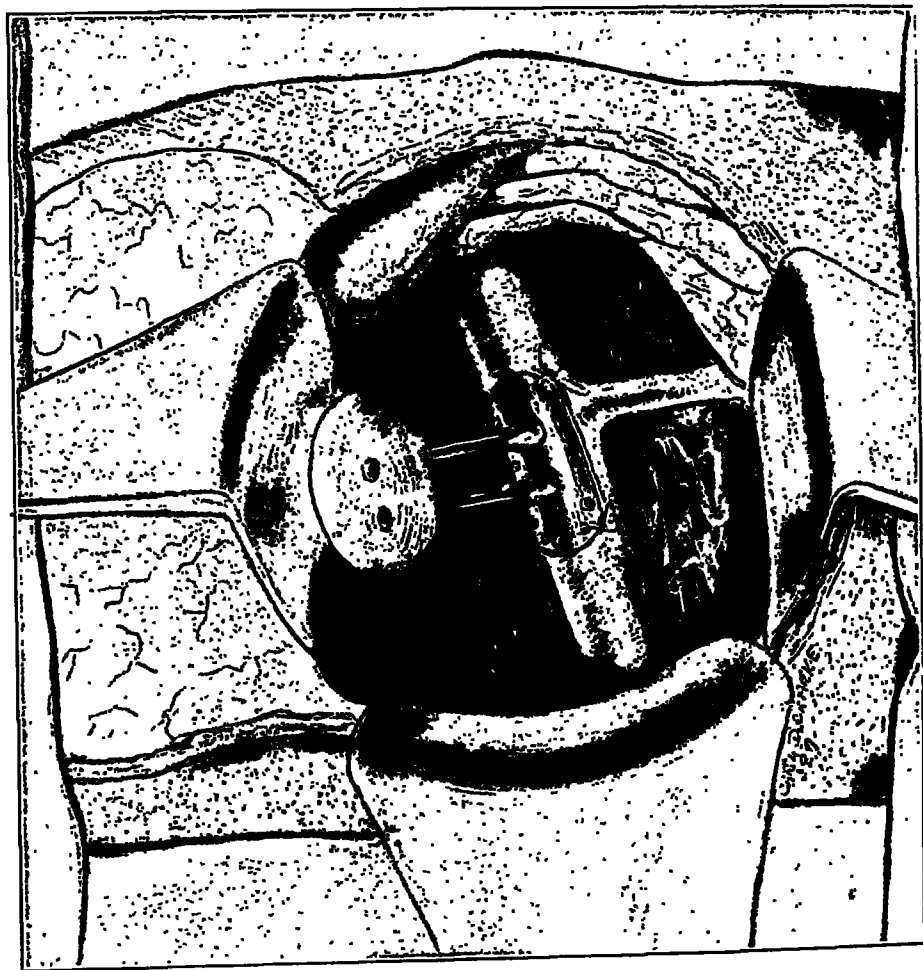


Fig. 5.—Instrument after it is sutured over the vein.

ASPIRATION OF THE BLOOD

The round plate of the cannula is grasped between the thumb and index finger. An 18 gage Record needle is passed through the skin into the depressed surface of the plate (*A*). The needle should be attached to a Record syringe and immediately after it is passed into the cannula, suction should be made with the piston of the syringe. If this technic is used, the portal blood will be aspirated into the syringe on the immediate entrance of the needle into the vein. After the desired quantity of blood is obtained, the needle is withdrawn from the vein, a distance of about one-fourth inch, and a stylet is placed in

the curved plate of the instrument (C) is sutured over the portal vein at the junction of the splenic vein. A curved incision is used to prevent the round plate of the instrument (A) from being placed beneath the scar of the incision. That portion (A) is therefore lateral to the incision. This can be seen in figure 3.

The illustration in figure 4 shows how the instrument is sutured over the portal vein. Four sutures are necessary to hold the instrument in place. It is better to apply all sutures before tying the knots.

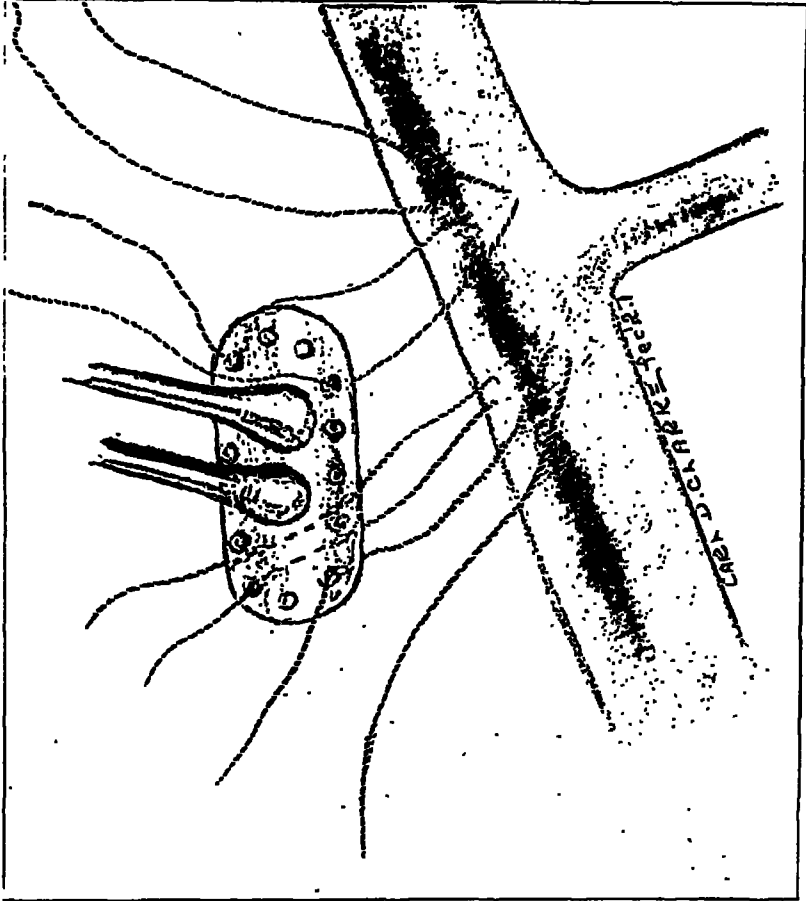


Fig. 4.—Illustration showing how instrument is sutured over the portal vein.

In figure 6 the instrument has been sutured over the vein. This has been done through the incision of the rectus muscle. The semicircular flap incision in the skin, and the plate (A) resting on the lower ribs should be noted.

The plate (A) is brought through the abdominal wall by making a second incision along the costal margin near the lower ribs. This incision includes the muscles and is not made through the skin. The instrument is suspended on the lower ribs to prevent pressure on the vein. The wound in the rectus muscle and peritoneum is closed; catgut is used in the peritoneum and silk in the sheath of the rectus muscle. The semicircular skin incision is sutured with interrupted sutures of silver wire.



Fig. 8.—A dog eighteen months after the introduction of the cannula. Blood may still be aspirated from the portal vein.

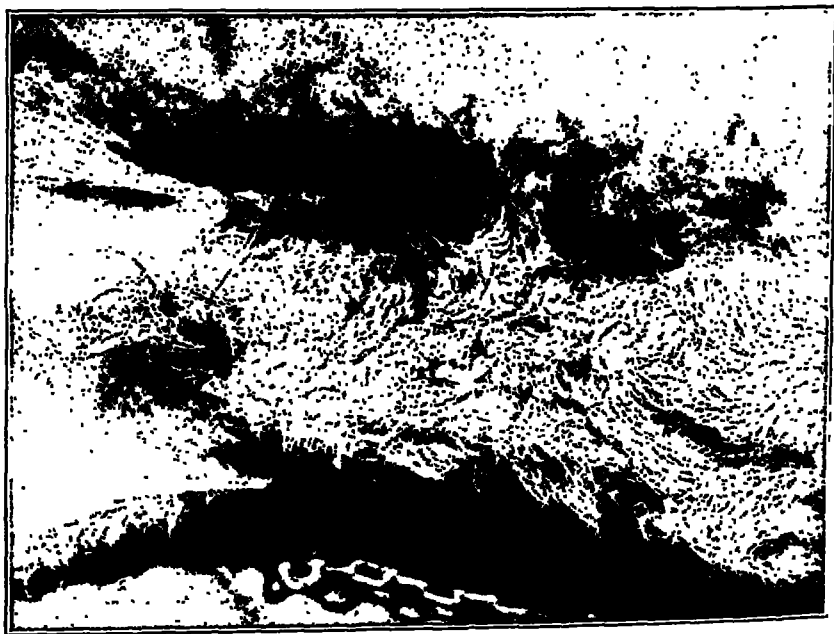


Fig. 9.—Close up view of the abdomen of the dog shown in figure 8. The arrow points to the instrument.

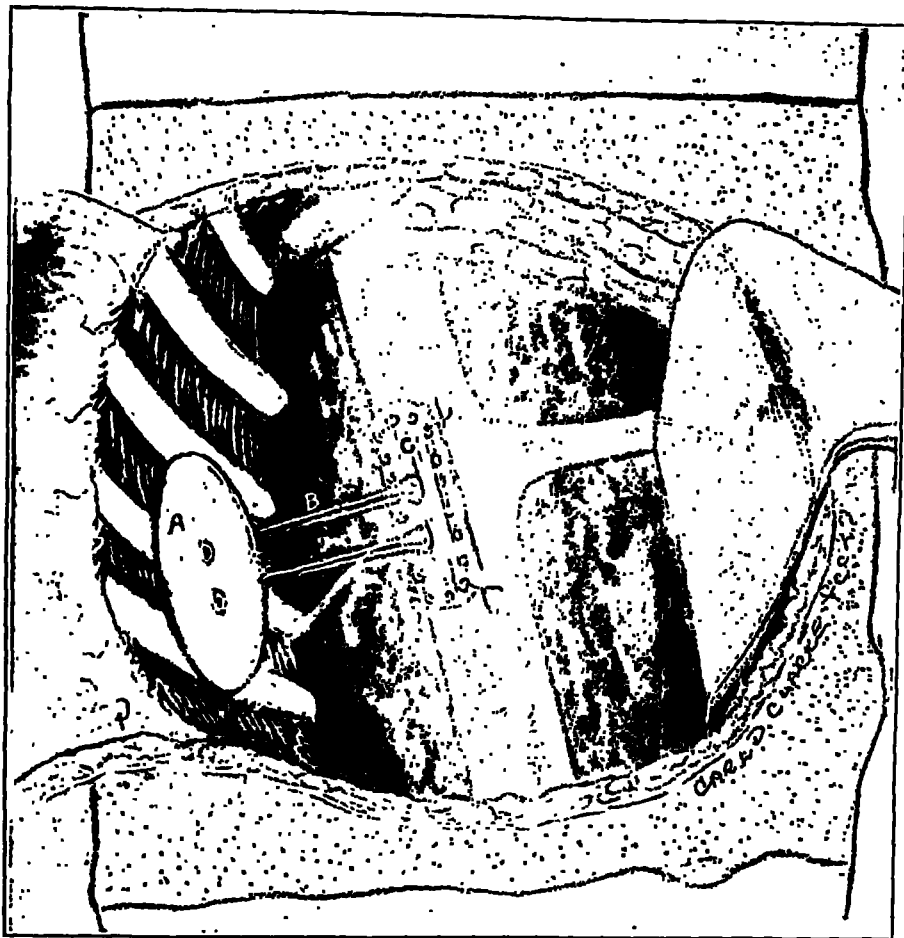


Fig. 6.—Instrument sutured over the vein by means of incision of the rectus muscle.



Fig. 7.—Close up view of the abdomen of the dog shown in figure 3. The scar of the semicircular skin incision and the plate of the instrument beneath the skin, as indicated by the arrow, should be noted.

TOXIC GOITER AND MENTAL DISEASE

RELIEF OF PSYCHOSES IN THYROTOXIC PATIENTS BY THYROIDECTOMY *

JOSEPH L. DECOURCY, M.D.

CINCINNATI

It has long been recognized that disturbances of the thyroid gland may give rise to mental disease, but hitherto attention has been focused largely on ablation of the thyroid function as the principal cause of thyrogenic psychoses. Before thyroid extract was employed, many patients with myxedema were confined in insane asylums. Without treatment, this disease may give rise to so extreme a degree of psychic paralysis that institutional care becomes necessary. Memory is lost, power of volition disappears, and the patient becomes completely indifferent to his surroundings. In cretinism, a somewhat similar train of mental symptoms follows.

The relation between toxic goiter and mental alienation is less generally admitted, yet I have made some observations that have led me to believe that under certain circumstances thyrotoxicosis may be the exciting, or at least a strong contributory, cause of serious mental disease, and that in such cases, particularly when the psychosis is not far advanced, operation may offer a good prospect of mental recovery. During the past five years I have performed thyroidectomy on fourteen frankly insane patients with toxic goiter; all but two recovered sufficiently to resume their former occupations.

LITERATURE

In 1908, Berkley and Follis¹ reported a study of a series of cases of the catatonic form of dementia praecox, in which they found a definite resemblance between symptoms of exophthalmic goiter and those of catatonia: chiefly, rapid pulse, muscular tremor, hyperhidrosis, over-active eye and other reflexes, rapid loss of weight, disturbance of the menses and vasomotor pareses. They observed that the psychic changes in the prodromal stage of catatonia also resemble those seen in exophthalmic goiter. In most of their cases of catatonia, the thyroid gland was found to be soft and mushy with occasional hard nodules. Usually it was not enlarged. Experiments showed that the administration of iodine, thyroid extract or desiccated thyroid woke the patients out of

* From the Department of Surgery, DeCourcy Clinic.

1. Berkley, H. J., and Follis, R.: An Investigation into the Merits of Thyroidectomy and Thyro-Lecithin in the Treatment of Catatonia, *Am. Med.-Psychol. Assoc.* 15:283, 1908.

the needle. This controls hemorrhage from the punctured wound of the vein. The needle is allowed to remain in this position for a few minutes and then may be withdrawn.

Several points should be emphasized in the application of this method besides those already mentioned. Cannulas of various sizes should be made that may be applicable to dogs of different sizes. It would be difficult to use an adjustable instrument. The instrument should be of sufficient length so that there will be neither pressure nor too much tension on the vein. The portal vein in the dog is freely movable, and too much tension by suspension of the instrument on the rib as already described is not likely to occur. If the needle is introduced as described and a stylet placed in the needle after aspirating the blood, hemorrhage will not occur. It is true that the use of a small needle may give rise to some difficulty by the formation of a clot in the needle. If this should occur, the needle may be withdrawn and cleansed or another needle may be used. It is possible that the needle may pass through the portal vein and enter the inferior vena cava. I am now using another separate plate directly over the vena cava, like the plate (C) of the instrument. This plate makes it impossible for the aspirating needle to penetrate the vena cava.

The method has been used successfully in ten dogs. Unlimited aspirations may be made. Figures 8 and 9 show a dog that has retained the instrument for eighteen months. The portal vein in this dog has been aspirated more than fifty times. The dog apparently is normal and has gained weight since the introduction of the cannula. In three of the dogs, the round plate of the cannula ulcerated through the skin in from six to eight months after the introduction of the cannula.

The cannula may be used in the study of absorption from the intestinal tract, in tests on the function of the liver and in the study of the various dyes in tests on the function of the liver by the introduction of these dyes directly into the portal vein.

thyroid gland compatible with the assumption of a thyroid origin of the mental disease. Morse,⁴ on the contrary, failed to find any uniform lesions in the thyroid gland in a series of twenty-seven postmortem examinations on patients with dementia praecox.

In 1910, Winslow⁵ reviewed the results obtained by Berkley and Follis and by Kanavel and reported five additional cases of dementia praecox in which partial thyroidectomy was performed. One of these patients died with acute thyroidism; two were greatly improved for a considerable period and then relapsed; one was not materially benefited; and one was improved, but could not be kept under observation. From these cases and the results reported by others, Winslow concluded that there seems to be some connection between the thyroid gland and catatonia; that partial thyroidectomy in the early stages of this disease has a favorable, and sometimes a curative, effect; but that, in the late stages, the operation does not have any beneficial results.

In 1922, Weinberg⁶ reported eight cases of mental disease with symptoms of hyperthyroidism and somewhat enlarged thyroid glands, but not the typical symptoms of exophthalmic goiter. Two of the patients had the manic-depressive type of psychosis; three, dementia praecox. Thyroidectomy was performed in three cases of this series, including one of the manic-depressive and one of the dementia praecox type, and resulted in complete relief from the mental symptoms.

In 1922, Eastman and Eastman⁷ stated:

Since all the clinical symptoms of Graves' disease are largely of nervous origin and all are emotional, many cases exhibiting rather definite forms of nervous and mental disease as mania, chorea, hysteria, etc., it is not at all surprising that the rather definite clinical syndrome of dementia praecox appears occasionally in connection with thyrotoxicosis.

They reported that at the Central Insane Hospital at Indianapolis, 101 consecutive patients with dementia praecox of all types were examined for signs of endocrine imbalance, and especially for thyroid hypertrophy. Of twenty-seven male patients, eleven, or 40 per cent, showed some degree of thyroid enlargement. Two of these patients had large goiters; six, a conspicuous enlargement of the gland; three, moderate hypertrophy of one or both lobes. Of seventy-four female patients, forty-eight, or 64 per cent, showed some thyroid hypertrophy. Eighteen

4. Morse, M. E.: *Pathologic Anatomy of Ductless Glands in Dementia Praecox*, J. Neurol. & Psychopath. 4:1, 1923.

5. Winslow, R.: *Partial Thyroidectomy in Dementia Praecox*, J. A. M. A. 55:1195 (Oct. 1) 1910.

6. Weinberg, H. M.: *Mental Side of Hyperthyroidism*, Penn. M. J. 25:618, 1922.

7. Eastman, J. R., and Eastman, N.: *Thyroid Surgery and Dementia Praecox Syndrome*, Ann. Surg. 76:438, 1922.

their stupor, so that they became talkative and excited and exhibited increased dermographia and hyperhidrosis, higher pulse rate and increased tendon reflexes.

A transitory amelioration of the mental symptoms has frequently been observed in cases of dementia praecox following thyroid medication, but lasting benefit has rarely been reported. Wagner-Jauregg,² however, noted a favorable influence from treatment with thyroid in some early cases of the hebephrenic type.

Berkeley and Follis performed partial ablation of the thyroid gland in ten cases of catatonia. Four of the patients recovered their mental equilibrium after operation; three improved slowly but progressively without a tendency to relapse. In one of these cases, the pathologic appearance of the thyroid gland was suggestive of exophthalmic goiter. The fourth patient improved rapidly for a time, but relapsed for a few months, during which period the remaining half of the thyroid gland increased in size. When this goiter again decreased in size, the mental condition became normal and remained so. In this case, no pathologic condition other than colloid goiter was found in the portion of the gland that was removed. In another case, there was less improvement but mental deterioration was more advanced, and only a small portion of the gland was removed. In four cases, there was slight fibrosis. Two of the patients were cured by the operation.

Kanavel³ reported the results of thyroidectomy in eleven cases of dementia praecox, eight of them of the catatonic type. All but two represented cases of from two to ten years' duration. Improvement in the mental condition was not noted after operation. Of the two recent cases of less than one year's duration, one occurred in a patient who had been operated on too recently to judge of the result. The other patient showed definite improvement, but not complete cure. Another case, not included in this series, was noted, in which the thyroid gland was removed because of symptoms of pressure due to enlargement. The operation resulted in marked mental improvement, so that the patient was discharged from institutional care and returned to work. In the eleven cases, ten of the thyroid glands removed were examined pathologically. Only two showed excessive parenchymatous growth; six showed colloid changes. Kanavel noted, however, that colloid glands may result from a degenerative change, and this observation does not absolutely exclude the assumption of a previously perverted excessive thyroidism. Eight of ten patients in this series showed changes in the

2. Wagner-Jauregg: *Organotherapie bei Neurosen und Psychosen*, Wien. klin. Wchnschr. 36:1, 1923.

3. Kanavel, A. B.: *The Advisability of Thyroidectomy in Catatonic Dementia Praecox*, Illinois M. J. 16:253, 1909.

sexes, goiter was most frequently associated with manic-depressive psychosis and dementia praecox. The goiters were chiefly of the adenomatous type; a few, of the colloid type. There were no goiters of the hyperplastic type, and evidence of hyperthyroidism was not present in any case. In a few cases the thyroid was removed, but without effect on the psychosis. In all instances, typical adenomatous changes were found in the removed gland. There were no cases of definite hyperthyroidism. In a study of 800 patients with goiter in a general hospital in the same locality, Foss and Jackson did not find any cases of true insanity. Only two patients showed mild excitement or slight and transient mania. Foss and Jackson, therefore, did not see any definite relationship between goiter and insanity, but they admit that thyroidectomy should be performed when there is evidence of hyperthyroidism in a person with a psychosis.

In 1923, Weiss¹¹ reported seven cases of psychoneurosis with anxiety states associated with definite symptoms of hyperthyroidism; that is, tachycardia tremor, glittering eyes and moist hands. Partial thyroidectomy in two cases, and roentgen-ray treatment of the thyroid gland in one case, failed to relieve the patient from the psychosis. Weiss believed that the thyrotoxicosis in these cases was not directly responsible for the mental symptoms, but that the two developed concomitantly, both as symptoms of an abnormal degenerative constitution, most probably with disturbance of the vegetative nervous system.

Studies of basal metabolism in dementia praecox indicate that a lowered rate is more frequent than high basal metabolism, which is characteristic of hyperthyroidism. In 1925, in a study of the basal metabolism in 161 cases of mental diseases of various types, Bowman and Fry¹² found that of twenty-four patients with dementia praecox, eighteen showed minus readings, which were abnormally low in seven instances. The manic-depressive group showed a tendency toward low readings in the depressive and hypomanic stages, but this was not so marked as in the cases of dementia praecox. In a review of the literature on basal metabolism in dementia praecox, Bowman and Fry found 125 cases (including their 24 cases). The basal metabolism was high in only eleven of the cases; in fifty-two, it was low, and in fifty-two, normal.

In 1921 and 1922, Lewis and Davies¹³ reported a study of twenty-two cases of dementia praecox in which the thyroid feeding test was

11. Weiss, R. F.: Psychoneurotische Störungen bei Hyperthyroidismus, *Ztschr. f. klin. Med.* **97**:366, 1923.

12. Bowman, K. M., and Fry, C. C.: Basal Metabolism in Mental Disease, *Arch. Neurol. & Psychiat.* **14**:819 (Dec.) 1925.

13. Lewis, N. D. C., and Davies, G. R.: Correlative Study of Endocrine Imbalance and Mental Diseases, *J. Nerv. & Ment. Dis.* **54**:385, 493, 1921; **55**:13, 1922.

of these had actual goiters, nine of which were apparently cystic. In both male and female patients, however, "the cardinal symptoms of thyrotoxicosis, except goiter, were notably absent." Eastman and Eastman reported four cases, all in females with the paranoid type of dementia praecox, in which one lobe of the thyroid or one lobe with the isthmus was enlarged. Two of the patients showed slight exophthalmos; the other two did not show any ocular signs of exophthalmic goiter. There were no frank symptoms of thyrotoxicosis, but all patients showed accelerated pulse rate and some tremor of the fingers. A hemithyroidectomy was performed in the four cases and in all the psychosis was entirely relieved, the patients returning to their usual occupations.

In 1924, Jackson⁸ reported a psychosis in a woman, aged 53, who had typical symptoms of exophthalmic goiter, although exophthalmos was slight. The thyroid gland was symmetrically enlarged to a slight degree. It felt firm and fibrous, being a typical hyperplastic gland. The right superior thyroid artery was first ligated. This operation resulted in a severe reaction with exacerbation of all the symptoms. Ligation of the left superior thyroid artery, however, resulted in marked improvement. Later, two thirds of the right lobe and isthmus were resected. Two weeks after this operation the basal metabolic rate fell to normal, and the patient was mentally normal.

In 1926, Boys⁹ stated that in his series of cases of toxic goiter he found that about 2 per cent show mental symptoms so severe that they may be called definite psychoses. He reported eight cases in which there were well developed mental symptoms and goiter. In six of these cases, removal of the thyroid gland resulted in complete recovery. The thyroid glands were grossly or microscopically hyperplastic, and the symptoms of hyperthyroidism had preceded the development of the psychosis. In one case there was an adenomatous goiter without hyperplasia, and in another, a simple colloid goiter. In neither of the cases were the mental symptoms improved by operation, nor had the symptoms of goiter preceded the development of the psychosis. One of the patients relieved by thyroidectomy was affected with the manic-depressive type of psychosis.

In 1924, Foss and Jackson¹⁰ reported an incidence of 59 cases of goiter among 1,647 patients at the State Hospital in Danville, Pa. As this institution is in a goiter belt, this is not a high incidence of goiter. Forty-nine of the goiters were in women; ten in men. In both

8. Jackson, A. S.: Value of Ligation in Psychosis of Exophthalmic Goiter, *Wisconsin M. J.* 22:426, 1924.

9. Boys, C. E.: Psychoses Associated with Goitre, *J. Michigan M. Soc.* 25: 653, 1926.

10. Foss, H. L., and Jackson, J. A.: Relationship of Goiter to Mental Disorders, *Am. J. M. Sc.* 167:724, 1924.

sanitarium in one of the suburbs, where she remained for a month. There was great physical improvement during this period; the weight increased and the pulse rate came down to normal.

She was then taken to her sister's home in Cincinnati, and immediately her mental condition began to become clear. Three months after the operation, her mind appeared entirely normal. The following month, she took a motor trip East by herself without suffering any mishap. She has been under observation for a year since that time and is now entirely well. Judging by her present condition, there is every reason to believe that she will remain so.

It would seem that in this case the mental disturbance belonged to the group of exhaustion psychoses. Apparently thyroidectomy, by removing the source of toxemia, was the essential factor in restoring mental balance.

CASE 2.—A white woman, aged 30, married, exhibited a mental disturbance characterized by a marked paranoid trend. For four years she had noticed a fulness in her neck. During the past year this growth had increased in size and she had become emotional and irritable. Since the birth of her last child fourteen months previously, she had lost 20 pounds (9 Kg.)

During the last three months the nervous symptoms had increased perceptibly, and her husband reported that at times her conduct was unusual. On one occasion she left home and was found late at night wandering in a nearby wood. She had loose, poorly organized delusions of persecution, such as are commonly observed in the paranoid type of dementia praecox. She believed that everybody was against her and feared that her husband was trying to kill her with poison. For this reason she refused to take medicine. The family history was negative with regard to mental disease and goiter.

On examination the patient appeared well developed but considerably below normal weight. She looked excited and apprehensive. Her appearance was typical of thyrotoxicosis. Her temperature was 99 F.; her pulse rate, from 130 to 140. The thyroid gland was about three times the normal size and of the consistency of a hyperplastic goiter.

After the usual preparation with a compound solution of iodine, thyroidectomy was performed. After one week she was taken home. Physical improvement was marked, but the mental derangement became worse. After about three months of treatment, however, during which time she ran away from home twice and frequently became so excited that hypnotics were required, she began to improve slowly. This improvement continued over a period of a year, at the end of which her mental status seemed normal. Eighteen months after operation, she was entirely well and her mental condition was clear.

The mental disturbance at the onset of the illness would suggest dementia praecox. In two other cases this diagnosis had actually been made and a poor prognosis given; yet both patients recovered completely after thyroidectomy.

SUMMARY

With the exception of the thyrogenic psychoses occasionally associated with myxedema and cretinism, it is generally held that a direct relationship does not exist between the thyroid gland and mental disease. Careful examination of the thyroid gland in cases of dementia praecox and other psychoses has failed to reveal any consistent anatomic changes.

performed. Evidence of hyperthyroidism was found in four cases. One of the patients showed definite symptoms of exophthalmic goiter. Thyroidectomy was performed in this case; but a change in the mental condition did not result, although physical symptoms were relieved. Two of the other patients with hyperthyroidism were fed with suprarenal gland; one, with suprarenal and pituitary gland. One of the patients showed marked improvement with regard to mental symptoms and was discharged as recovered. In twelve cases of this series there was definite evidence of hypothyroidism. The thyroid feeding test was found to be of definite value in distinguishing between cases of hyperthyroidism and hypothyroidism.

RESULTS

During the past five years, I have operated on fourteen mentally unbalanced patients with toxic goiter. The mental symptoms were extremely pronounced in the majority of cases, yet all but two patients recovered completely and were able to resume their former occupations. They have remained clear mentally to date.

In two instances, both in young persons, a diagnosis of dementia praecox was made and a poor prognosis given; yet both patients recovered. In all but one case, the derangement occurred in persons suffering from the exophthalmic type of goiter. The exception was a case of the toxic adenomatous type, also with evidence of hyperplasia.

The period during which mental recovery took place varied from several months to a year. Two patients with dementia were not improved by operation; one died in an asylum, the other is still an inmate. In one case, a psychosis developed on the eighth day following removal of an extremely toxic goiter, and this patient is still in a sanitarium.

REPORT OF CASES

CASE 1.—A white woman, aged 35, single, was first seen at the Connecticut State Insane Asylum, Middletown, Conn., when she was in a highly excited state and could not orient herself as to time or place. During the preceding six months, she had lost 40 pounds (18.1 Kg.).

Examination revealed an enlarged thyroid gland, of the consistency found in hyperplastic goiter, with an adenoma about the size of an egg overlying the right lobe. Tremor was pronounced. The pulse rate varied between 140 and 160 and was weak.

The patient was removed to the Good Samaritan Hospital, Cincinnati, being accompanied on the trip by her sister and a nurse. During the journey she made several attempts to leave the train and was continually muttering unintelligibly. While in the hospital at Cincinnati, she tried several times to eat her own feces.

With rest and the administration of a compound solution of iodine she began to improve physically, but her mental condition remained the same. Two weeks after her arrival, thyroidectomy was performed. The reaction was slight and the postoperative course uneventful. Following operation, she was removed to a

VITAL CAPACITY

ITS SIGNIFICANCE IN RELATION TO POSTOPERATIVE PULMONARY COMPLICATIONS *

JOHN H. POWERS, M.D.

BOSTON

Determinations of vital capacity, heretofore utilized chiefly by physiologists or restricted to the study of serious cardiac or pulmonary disabilities, are now finding a wider application. The ease with which this accurate information is accumulated has greatly facilitated the dissemination of its practical value.

The determination of the vital capacity of any given patient is clearly one method of appraising the condition present. Any disorder which affects the cardiovascular or respiratory systems reduces the vital capacity. Such determinations may be of use not only in the diagnosis of these cardiorespiratory afflictions, but they also may be of assistance in determining the fitness of any given person. This may be utilized in surgical procedures to appraise the ability of a patient to withstand an operation. Since so many operations of today are those of election, the acquisition of this information seems desirable. Accurate knowledge of pulmonary and cardiac reserve energy might prove to be of inestimable value in deciding on the operability of patients before subjecting them to prolonged procedures. It would seem especially applicable to elderly or debilitated patients and to those whose past history reveals evidence of previous cardiac or pulmonary pathologic conditions. Already articles have appeared relative to the effect of certain surgical conditions and different types of operative incisions on the vital capacity. These latter studies are of great importance since they give a rough estimate of the reduction that follows certain incisions, the position of which interferes with free respiration. Such studies create normal base lines below which further reductions have a deeper significance.

The startling increase in the number of postoperative pulmonary complications during the past two decades points to the importance of making accurate observations during the convalescent period. Pfannenstiel,¹ in 1903, and Otte,² in 1907, reported large series of cases in which postoperative pulmonary complications were not observed, a

* From the Surgical Clinic of the Lakeside Hospital, Cleveland.

1. Pfannenstiel, J.: Ueber die Vorzüge der Äthernarkose, *Zentralbl. f. Gynäk.* 1:8, 1903.

2. Otte, A.: Ueber die postoperativen Lungenkomplikationen und Thrombosen nach Aethernarkosen, *München. med. Wchnschr.* 54:2473, 1907.

However, toxic goiter is sometimes observed in association with serious mental diseases, and experience has proved that in such cases, not only the physical condition, but the psychosis as well, may be benefited materially by thyroidectomy. When the mental disturbance is of recent onset and the thyrotoxic manifestations are severe, a fair prospect of mental recovery may be offered following thyroidectomy.

My experience in the treatment for combined toxic goiter and mental alienation comprises fourteen cases, in which I performed thyroidectomy during the past five years. Although the mental symptoms were extremely pronounced in the majority of these cases, all but two of the patients recovered mentally and were able to resume their former occupations, remaining normal to date. In two of the cases, the diagnosis of dementia praecox had been made and a poor prognosis given, yet both patients recovered. In all but one instance, the goiter was of the exophthalmic type; the exception was a toxic adenomatous goiter with evidence of hyperplasia. When thyroidectomy is performed on patients with psychoses, preoperative rest, medication with a compound solution of iodine and the most perfect operative technic are perhaps even more important than in patients with normal mentality.

dence of a pathologic process in the chest could well have escaped recognition.

Even such an extensive lesion as massive atelectasis of one lung passed unrecognized for many years by physicians and surgeons alike. The condition was first described by Pasteur¹¹ in 1908, but the first cases of postoperative collapse to be reported in the American literature did not appear until 1921.¹²

These studies on the vital capacity of surgical patients were undertaken with the hope of establishing a means of detecting transient, minor postoperative upsets and corroborating the diagnosis of gross pulmonary complications.

METHOD

Dr. Francis Peabody¹³ stated:

"The vital capacity of the lungs consists of the volume of the deepest possible expiration after the greatest possible inspiration. A certain amount of air, known as the residual air, remains in the lungs after complete expiration but the vital capacity represents the degree of movability of the lungs and anything which interferes with the movement of the lungs, preventing the entrance of the air into them, causes a decrease in the vital capacity."

Any acute process in the abdomen producing reflex spasm of the abdominal musculature involves the accessory muscles of respiration and hence inhibits respiratory excursion. Likewise, any operative procedure attended subsequently by splinting of the abdomen has a direct influence on the vital capacity. Consequently, it was necessary first to establish normal curves in order to determine the reduction in vital capacity following the various types of operative procedures in uncomplicated cases.

All the male patients admitted to the surgical service of the Lakeside Hospital were studied during a period of several months. At first the female patients were included, but the men were found to be more cooperative and the results accordingly more satisfactory. All the patients were encouraged to exert themselves to the utmost in spite of pain, and a friendly spirit of rivalry was stimulated in the ward, each man trying to "blow harder" than his neighbor in the next bed. Whenever it was felt that a patient was not cooperating fully, his observations were discarded.

The Collins Vital Capacity Spirometer was used. It consists of a delicately compensated bell floating in a cylinder of water. The most essential feature of the apparatus is the direct reading dial which is graduated to tenths of liters. Fractions of these graduations may be estimated in tenths also. As the bell rises with expiration, a movable pointer passes over the face of the dial, stops at the highest point and remains in that position. A second pointer is connected with the dial which is of value if the patient tends to inspire from the spirometer just before expiring into it. In such a case, the bell may be raised and the pointers adjusted so that both are at the 1 liter mark. If the

11. Pasteur, W.: Massive Collapse of the Lung, *Lancet* 2:1351, 1908.

12. Scrimger, F. A. C.: Postoperative Massive Collapse of the Lung, *Surg. Gynec. Obst.* 32:486, 1921.

13. Peabody, F. W.: The Clinical Importance of the Vital Capacity of the Lungs, *Northwest Med.* 22:307, 1923.

remarkable and praiseworthy record. In the light of present knowledge, however, it is possible that a reexamination of the individual case reports might reveal minor symptoms indicative of transient pulmonary complications.

In 1906, Armstrong³ reported a pulmonary morbidity of 2.12 per cent in 2,500 cases at the Montreal General Hospital. In 1908, von Lichtenberg⁴ collected 23,673 cases with a pulmonary morbidity of 1.9 per cent. The same year, Ranzi⁵ published 263 pulmonary complications from 6,871 operations in von Eiselberg's Clinic at Vienna, a morbidity of 3.8 per cent. Beckman⁶ reported the pulmonary complications at the Mayo Clinic in 1910, 1912 and 1913. When his figures are amended to include pulmonary embolism, they reveal morbidities of 1.12 per cent, 1.57 per cent and 1.27 per cent, respectively. Cutler and Morton⁷ found 1.86 per cent of cases in 3,490 operations at the Massachusetts General Hospital in 1917. One year later, McKesson⁸ computed 3.03 per cent of pulmonary complications from the combined statistics of 39,438 operations. In 1920, Cutler and Hunt⁹ reported a pulmonary morbidity of 3.52 per cent in 1,562 patients operated on at the Peter Bent Brigham Hospital, and the following year,¹⁰ 3.92 per cent in 1,604 cases at the same hospital.

It seems probable that a more careful analysis of all these statistics would reveal not actually a greater number of postoperative complications during recent years, but a more astute recognition and correct interpretation of symptoms which heretofore have passed unnoticed. A slight unexplained fever, a transient cough with or without thoracic pain, a few flecks of blood-tinged sputum without gross clinical evi-

3. Armstrong, G. E.: Lung Complications After Operations with Anesthesia, *Brit. M. J.* 1:1141, 1906.

4. Von Lichtenberg, A.: Die postoperativen Lungenkomplikationen, *Centralbl. f. d. Grenzgeb. d. Med. u. Chir.* 11:129, 1908.

5. Ranzi, E.: Ueber postoperative Lungencomplicationen embolischer Natur, *Arch. f. klin. Chir.* 87:380, 1908.

6. Beckman, E. H.: Pulmonary and Circulatory Complications Following Surgical Operations, *Collected Papers Mayo Clinic, Philadelphia, W. B. Saunders Company, 1910, pp. 594-599; Complications Following Surgical Operations, ibid., 1912, pp. 738-745; Complications Following Surgical Operations, ibid., 1913, pp. 776-788.*

7. Cutler, E. C., and Morton, J. J.: Postoperative Pulmonary Complications, *Surg. Gynec. Obst.* 25:621, 1917.

8. McKesson, E. I.: Some Observations on Postoperative Lung Complications, *Am. J. S. (Anes. Supp.)* 32:16, 1918.

9. Cutler, E. C., and Hunt, A. M.: Postoperative Pulmonary Complications, *Arch. Surg.* 1:114 (July) 1920.

10. Cutler, E. C., and Hunt, A. M.: Postoperative Pulmonary Complications, *Arch. Int. Med.* 29:449 (April) 1922.

Chart 4 represents the average vital capacity and temperature of five patients who were subjected to upper abdominal operations. Table 4 presents the daily readings in detail. The third patient in the series had a perforated gastric ulcer. On admission, there was marked

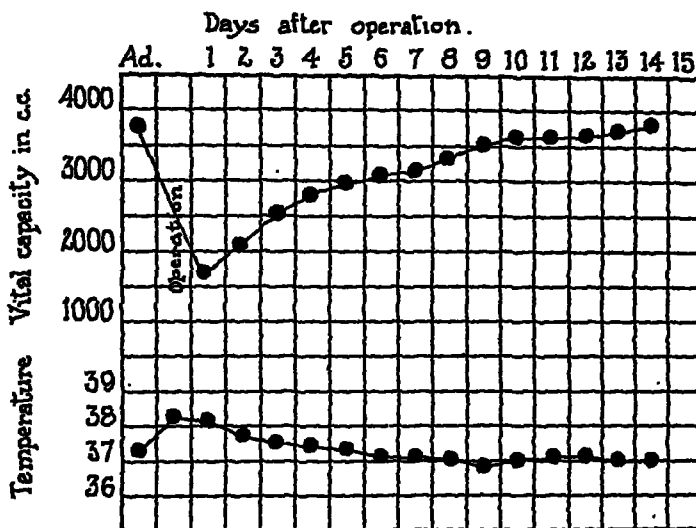


Chart 1.—Composite curve showing the vital capacity of eight patients who were operated on for bilateral inguinal hernia.

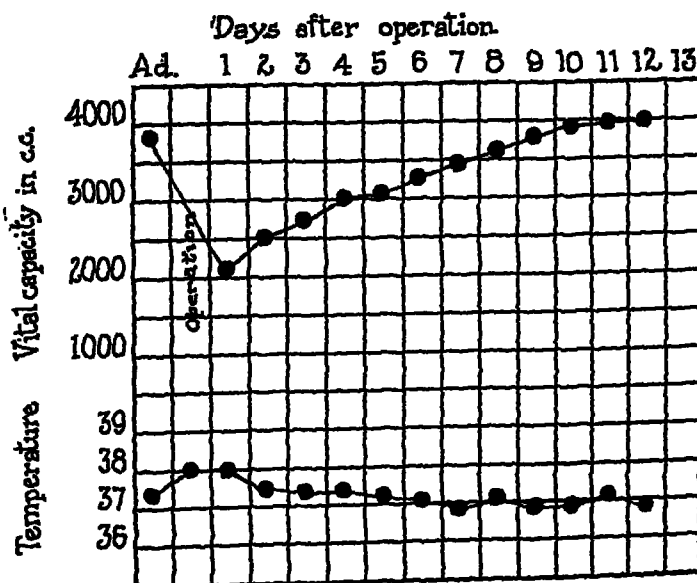


Chart 2.—Curve showing the vital capacity and temperature in eight uncomplicated cases in which operation for unilateral inguinal hernia was performed.

spasm of the whole abdomen and likewise a striking decrease in the vital capacity, 1,800 cc. compared with 5,420 cc. on the fifteenth post-operative day.

patient inspires from the apparatus before expiring, one pointer moves toward the zero mark until inspiration ceases. The other moves in a clockwise direction with expiration. In this case, the difference between the two pointers represents the vital capacity of the lungs. The calibration of the apparatus is exact and the breathing tube is sufficiently large to prevent resistance to expiration.

A nose clip was not used; the patient was instructed to close his nose by gentle pressure of the thumb and finger. Whenever leakage occurred, it could be easily detected by fogging on the polished metal surface of the mouthpiece.

All observations were made with the patients in the recumbent position and are accordingly slightly lower than the average recorded for patients of equal height and weight in the erect posture.¹⁴ They were also taken at least two hours after a meal in order to obviate the possible inhibitory effect of abdominal distention.

The vital capacity was taken on admission and daily throughout the post-operative convalescent period, until a high level was reached or the patient discharged.

The highest of three to five observations was chosen as the most accurate. A record was kept of the operative procedure, the type and the duration of the anesthetic. There were no untoward wound results, even in patients with several drains in the abdomen. Clean wounds healed firmly by primary union as usual. A careful clinical record was kept throughout the patient's sojourn in the hospital and correlated with the vital capacity each day. As an index of the patient's general condition the temperature curve has been plotted beneath the vital capacity.

OBSERVATIONS ON NORMAL PATIENTS

All the similar types of cases have been grouped together. The preoperative level in each has been arbitrarily regarded as 100 per cent and the daily reductions calculated in percentages of this figure.

Chart 1 represents the composite curve of eight uncomplicated operations for bilateral inguinal hernia. Table 1 gives the daily readings for each patient in detail with the average and percentage calculated below.

Chart 2 is a record of the vital capacity and temperature in eight uncomplicated operations for unilateral inguinal hernia. Table 2 is a detailed representation of the daily readings for each patient with the average and percentage calculated below.

Chart 3 and table 3 are representative of eight patients operated on through a McBurney incision for acute appendicitis. The higher readings during the latter days of the convalescence indicate a diminished vital capacity on admission. This was undoubtedly caused by the limitation of respiratory excursion incidental to an acute process in the abdomen.

14. Christie, C. D., and Beams, A. J.: The Estimation of Normal Vital Capacity, *Arch. Int. Med.* 30:34 (July) 1922.

of fingers and toes, incision and drainage of osteomyelitis, incision, drainage and arthrodesis of joints.

Some interesting results were obtained in patients subjected to thyroidectomy. Chart 9 shows an immediate and striking reduction in

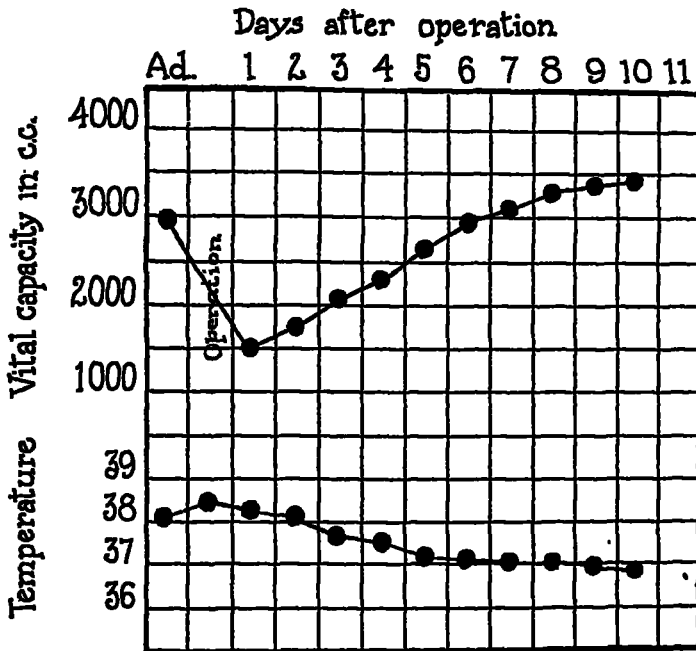


Chart 3.—Vital capacity of eight patients on whom appendicectomy was performed (McBurney).

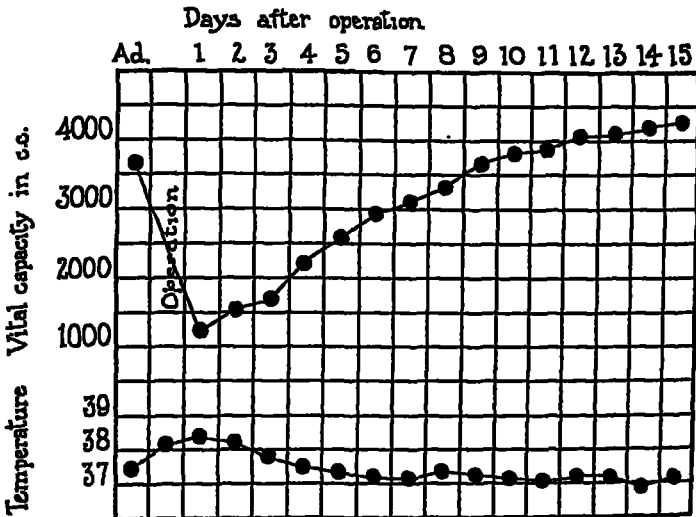


Chart 4.—Average vital capacity and temperature of five patients who were subjected to operation on the upper part of the abdomen.

vital capacity followed by a rapid recovery. Table 8 is a detailed analysis of each case.

Other operations on the neck have only a slight effect on the vital capacity. This lies within the limits of normal daily variation and

There was only one uncomplicated operation involving a midline incision in the lower part of the abdomen. Resection of the bladder and transplantation of the ureters into the rectum were performed for carcinoma of the bladder. This curve is presented in chart 5.

Seven patients were operated on for hydrocele. A slight reduction in the vital capacity occurred during the first few days after operation, in spite of the fact that the aponeurosis of the external oblique was not

TABLE 1.—*Vital Capacity of Patients Operated On for Bilateral Inguinal Hernia Given in Cubic Centimeters*

| On Admis- sion | Days After Operation | | | | | | | | | | | | | |
|----------------------|----------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
| 3,560 | 2,250 | 2,600 | 2,950 | 2,900 | 3,050 | 3,230 | 3,150 | 3,000 | 3,250 | 3,200 | 3,550 | 3,700 | 3,660 | 3,700 |
| 3,300 | 1,720 | 2,200 | 2,580 | 2,310 | 2,630 | 2,720 | 2,900 | 3,020 | 3,150 | 3,100 | 3,400 | 3,500 | 3,410 | 3,520 |
| 5,000 | 2,440 | 2,700 | 3,800 | 4,200 | 4,320 | 4,450 | 3,900 | 4,450 | 4,800 | 5,020 | 4,150 | 3,900 | 4,500 | 4,550 |
| 2,350 | 1,900 | 1,980 | 2,100 | 2,500 | 2,530 | 2,600 | 2,730 | 2,740 | 2,720 | 2,800 | 2,810 | 2,920 | 2,930 | 2,930 |
| 3,500 | 1,000 | 1,000 | 1,320 | 1,740 | 1,800 | 2,120 | 2,680 | 2,990 | 3,000 | 3,180 | 3,400 | 3,500 | 3,500 | 3,500 |
| 3,900 | 1,000 | 1,780 | 1,810 | 2,600 | 2,720 | 2,700 | 2,800 | 3,100 | 3,580 | 3,750 | 3,550 | 3,600 | 3,600 | 3,910 |
| 3,880 | 1,700 | 1,820 | 2,140 | 2,310 | 2,510 | 2,790 | 3,120 | 3,200 | 3,350 | 3,380 | 3,850 | 3,800 | 3,510 | 3,610 |
| 4,600 | 1,550 | 2,950 | 3,500 | 3,700 | 3,810 | 4,010 | 4,060 | 4,300 | 4,100 | 4,430 | 4,600 | 4,600 | 4,700 | 4,750 |
| 3,761 | 1,635 | 2,141 | 2,525 | 2,809 | 2,921 | 3,077 | 3,167 | 3,350 | 3,506 | 3,629 | 3,006 | 3,627 | 3,734 | 3,846 |
| 100% | 45% | 57% | 67% | 74% | 77% | 81% | 84% | 89% | 93% | 95% | 95% | 96% | 96% | 102% |

TABLE 2.—*Unilateral Inguinal Hernia*

| On Admis- sion | Days After Operation | | | | | | | | | | | |
|----------------------|----------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| 3,800 | 1,740 | 1,950 | 2,210 | 2,810 | 3,190 | 3,300 | 3,420 | 3,680 | 3,900 | 3,850 | 3,900 | 3,910 |
| 3,900 | 3,570 | 3,400 | 3,310 | 3,410 | 3,610 | 3,900 | 3,930 | 4,110 | 4,190 | 4,270 | 4,200 | 4,200 |
| 3,690 | 2,050 | 2,300 | 2,710 | 3,070 | 3,220 | 3,520 | 3,500 | 3,600 | 3,600 | 3,710 | 3,770 | 3,820 |
| 3,550 | 1,820 | 2,740 | 2,990 | 3,240 | 3,140 | 3,450 | 3,570 | 3,670 | 3,700 | 3,750 | 3,760 | 3,760 |
| 3,000 | 1,700 | 2,150 | 2,590 | 2,640 | 2,710 | 2,800 | 3,000 | 2,960 | 3,200 | 3,250 | 3,300 | 3,600 |
| 5,300 | 2,840 | 3,320 | 3,820 | 3,710 | 3,700 | 4,060 | 4,300 | 4,790 | 4,090 | 5,220 | 5,300 | 5,190 |
| 3,800 | 2,500 | 2,800 | 3,300 | 3,350 | 2,820 | 3,320 | 3,400 | 2,480 | 2,690 | 3,800 | 3,870 | 3,890 |
| 3,980 | 1,640 | 2,040 | 2,400 | 2,400 | 2,550 | 2,450 | 3,090 | 3,260 | 3,620 | 3,880 | 3,820 | 3,900 |
| 3,250 | 1,630 | 1,820 | 2,100 | 2,380 | 2,630 | 2,910 | 3,160 | 3,120 | 3,320 | 3,300 | 3,400 | 3,400 |
| 3,608 | 2,188 | 2,505 | 2,709 | 3,000 | 3,090 | 3,319 | 3,489 | 3,630 | 3,791 | 3,902 | 3,924 | 3,991 |
| 100% | 57% | 65% | 72% | 78% | 81% | 87% | 91% | 95% | 99% | 102% | 103% | 104% |

incised. Curves are represented in chart 6 and daily readings are given in detail in table 5.

Rectal operations, including hemorrhoidectomies, excision of fistulas, incision and drainage of ischiorectal abscesses, do not produce any postoperative reduction in vital capacity. Chart 7 is a composite curve of the vital capacity and temperature of eight patients. Table 6 presents the daily observations in detail.

Operations on the extremities likewise do not have any appreciable effect on the vital capacity other than that which can be explained on the basis of daily variation; (chart 8, table 7). Fifteen patients were studied. The operations include excision of varicose veins, amputations

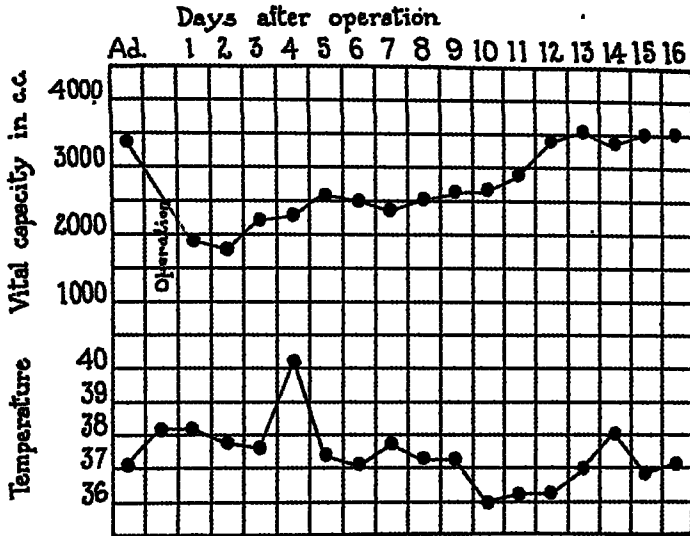


Chart 5.—Vital capacity of one patient following resection of the bladder and transplantation of the ureters.

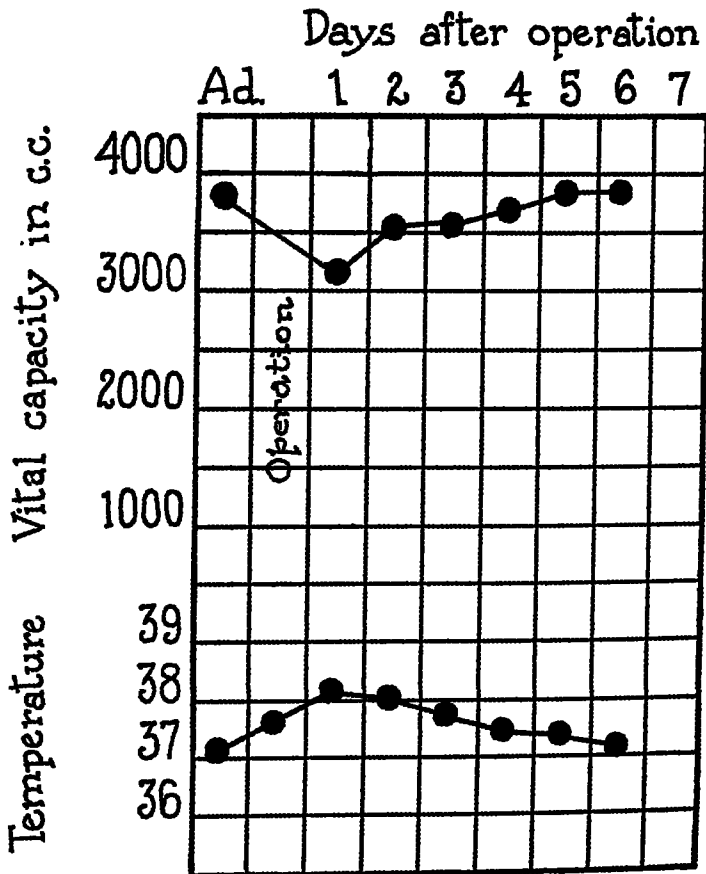


Chart 6.—Vital capacity of seven patients operated on for hydrocele.

probably has no bearing on the operative procedure. The four cases include excision of tuberculous glands, incision and drainage of an abscess, and radical dissection (chart 10, table 9).

OBSERVATIONS ON PATIENTS WITH POSTOPERATIVE COMPLICATIONS

There were no complications among the patients operated on for bilateral inguinal hernia.

Chart 11 is a graph of the vital capacity and temperature of a healthy man, aged 26, who was operated on for right inguinal hernia under gas-oxygen-ether anesthesia. The usual reduction in vital

TABLE 3.—*Acute Appendicitis (McBurney Incision)*

| On Admis- sion | Days After Operation | | | | | | | | | |
|----------------------|----------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| 2,540 | 1,420 | 1,350 | 1,850 | 1,910 | 2,100 | 2,500 | 2,660 | 2,820 | 2,820 | 2,800 |
| 1,820 | 1,410 | 1,460 | 1,590 | 1,720 | 1,900 | 2,100 | 2,400 | 2,800 | 2,910 | 2,910 |
| 3,120 | 1,360 | 1,400 | 1,580 | 1,700 | 2,100 | 2,350 | 3,000 | 2,850 | 3,160 | 3,150 |
| 4,050 | 1,550 | 1,840 | 2,310 | 2,600 | 3,080 | 3,460 | 3,610 | 3,820 | 4,060 | 4,200 |
| 3,480 | 1,680 | 1,940 | 2,090 | 2,850 | 3,430 | 3,610 | 3,760 | 4,030 | 4,100 | 4,100 |
| 3,000 | 2,060 | 2,580 | 2,970 | 3,310 | 3,510 | 3,680 | 3,830 | 3,950 | 3,950 | 3,900 |
| 2,110 | 1,710 | 1,900 | 1,980 | 2,040 | 2,300 | 2,340 | 2,600 | 2,450 | 2,600 | 2,600 |
| 3,100 | 1,080 | 2,080 | 2,490 | 2,910 | 3,150 | 3,510 | 3,510 | 3,710 | 3,700 | 3,710 |
| 2,977 | 1,534 | 1,819 | 2,108 | 2,380 | 2,696 | 2,944 | 3,184 | 3,304 | 3,413 | 3,436 |
| 100% | 52% | 61% | 70% | 79% | 90% | 93% | 106% | 110% | 114% | 115% |

TABLE 4.—*Operations on the Upper Part of the Abdomen*

| On Admis- sion | Days After Operation | | | | | | | | | | | | | | |
|----------------------|----------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
| 3,680 | 900 | 1,300 | 1,100 | 1,760 | 2,800 | 3,000 | 2,850 | 3,390 | 3,750 | 3,650 | 3,700 | 3,750 | 3,750 | 3,750 | 3,750 |
| 3,880 | 1,690 | 1,950 | 2,450 | 2,760 | 2,720 | 2,880 | 3,000 | 3,230 | 3,500 | 3,450 | 3,500 | 3,760 | 3,520 | 3,900 | 3,900 |
| 1,900 | 1,350 | 2,460 | 2,840 | 3,410 | 3,720 | 4,460 | 5,180 | 4,950 | 5,210 | 5,370 | 5,880 | 5,420 | 5,420 | 5,410 | 5,420 |
| 3,880 | 1,050 | 980 | 1,300 | 1,640 | 1,760 | 2,080 | 2,200 | 2,500 | 2,790 | 2,950 | 2,980 | 3,050 | 3,210 | 3,320 | 3,300 |
| 5,430 | 1,250 | 1,060 | 950 | 1,760 | 2,150 | 2,230 | 2,720 | 2,820 | 3,160 | 3,590 | 3,820 | 4,350 | 4,520 | 4,730 | 5,100 |
| 3,624 | 1,248 | 1,550 | 1,724 | 2,266 | 2,530 | 2,924 | 3,180 | 3,384 | 3,682 | 3,802 | 3,876 | 4,066 | 4,084 | 4,222 | 4,204 |
| 100% | 34% | 43% | 48% | 63% | 70% | 81% | 88% | 93% | 101% | 103% | 107% | 112% | 112% | 116% | 118% |

capacity occurred on the first postoperative day. When the observations were taken on the forenoon of the second day a marked secondary reduction was found. During the early afternoon, the patient developed acute respiratory distress; temperature, pulse and respirations were elevated, and physical examination of the chest revealed a massive atelectasis on the right side. This was confirmed by a roentgenogram. On the third day, a slight increase in vital capacity and fall in temperature were observed. On the fourth day, the vital capacity was again reduced and the temperature elevated. Following this, both rapidly returned to normal (compare with chart 2).

Chart 12 is most interesting. The patient was a well developed, but somewhat plethoric man, aged 44, who had suffered with chronic asthma

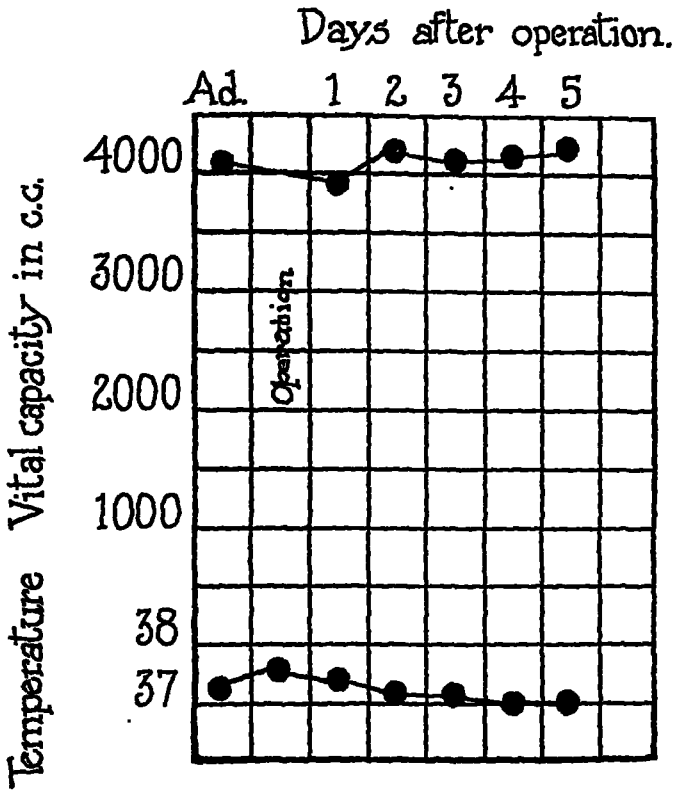


Chart 7.—Composite curve of the vital capacity and temperature of eight patients on whom rectal operations were performed.

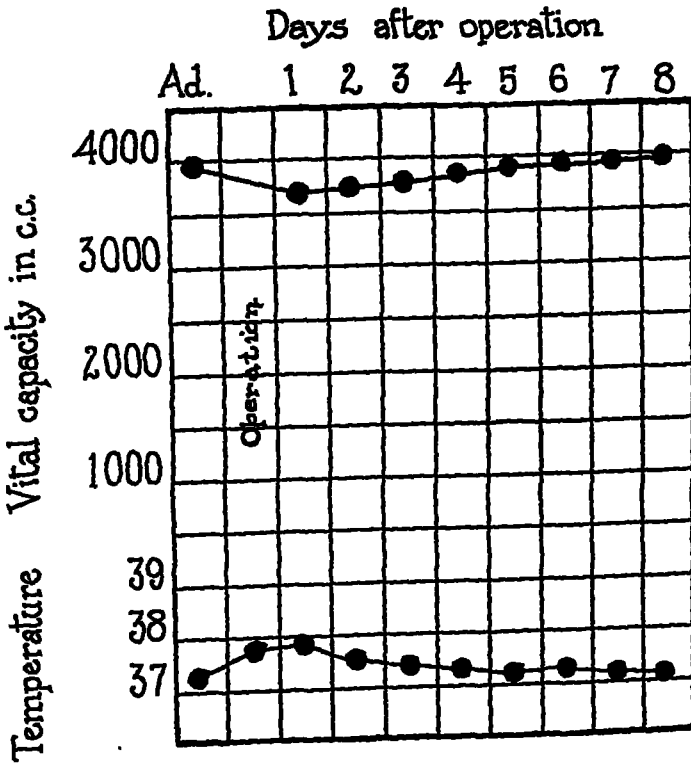


Chart 8.—Vital capacity of fifteen patients who were subjected to operations on the extremities.

for many years. Examination of the chest revealed typical asthmatic symptoms; clubbing of the fingers and toes was present. The pre-operative vital capacity was only 2,650 cc., 64 per cent of the expected normal for a man of corresponding height and weight. A right inguinal hernia was repaired under local infiltration and block anesthesia with procaine hydrochloride. The usual reduction in vital capacity occurred on the first postoperative day, accompanied by a marked elevation in temperature. During the subsequent four days, the vital capacity increased slowly, but the temperature remained elevated. On the sixth day, a decrease in vital capacity was noted. During the next three

TABLE 5.—*Hydrocele*

| On Admission | Days After Operation | | | | | |
|--------------|----------------------|-------|-------|-------|-------|-------|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| 4,660 | 4,100 | 4,160 | 4,200 | 4,680 | 4,680 | 4,660 |
| 3,610 | 3,170 | 3,290 | 3,140 | 3,800 | 3,850 | 3,550 |
| 3,800 | 2,500 | 2,700 | 2,950 | 3,200 | 3,510 | 3,510 |
| 3,470 | 3,140 | 3,500 | 3,550 | 3,550 | 3,550 | 3,550 |
| 4,500 | 4,200 | 4,700 | 4,520 | 4,600 | 4,600 | 4,600 |
| 3,560 | 2,200 | 3,280 | 3,310 | 3,520 | 3,620 | 3,400 |
| 2,980 | 3,140 | 3,120 | 3,340 | 3,320 | 3,340 | 3,340 |
| 3,797 | 3,207 | 3,536 | 3,573 | 3,739 | 3,807 | 3,853 |
| 100% | 84% | 93% | 94% | 98% | 100% | 101% |

TABLE 6.—*Rectal Operations*

| On Admission | Days After Operation | | | | |
|--------------|----------------------|-------|-------|-------|-------|
| | 1 | 2 | 3 | 4 | 5 |
| 4,290 | 4,080 | 4,590 | 4,530 | 4,550 | 4,590 |
| 3,170 | 3,500 | 4,170 | 4,200 | 4,210 | 4,350 |
| 3,680 | 3,600 | 3,680 | 3,670 | 3,690 | 3,680 |
| 4,210 | 4,120 | 4,250 | 4,100 | 4,100 | 4,170 |
| 4,480 | 4,680 | 5,000 | 4,800 | 4,000 | 4,050 |
| 4,300 | 4,820 | 4,320 | 4,500 | 4,440 | 4,440 |
| 4,480 | 4,100 | 4,560 | 4,510 | 4,500 | 4,500 |
| 3,820 | 3,120 | 3,450 | 3,420 | 3,450 | 3,450 |
| 4,116 | 3,940 | 4,252 | 4,216 | 4,238 | 4,274 |
| 100% | 93% | 103% | 102% | 103% | 104% |

days, the vital capacity continued steadily downward, the temperature rose slightly, and the patient showed clinical signs of bronchopneumonia. This diagnosis was confirmed by the roentgen-ray examination. Recovery was extremely slow. The temperature remained elevated until the twenty-seventh postoperative day and the vital capacity did not attain its preoperative level until the twenty-ninth day.

In spite of this stormy convalescence, the patient wished to have a left femoral hernia repaired before leaving the hospital. After the temperature had been normal for several days, this operation was performed under local and block anesthesia as before. The usual reduction in vital capacity occurred on the first postoperative day and a marked

and the temperature rose to 39 C. (102.1 F.). The physical examination was negative. The following day, the temperature was 40.6 C. (105 F.) and the vital capacity 820 cc. The physical examination and roentgenogram revealed pleurisy with effusion at the base of the right lung. Thoracentesis was performed twice during the next five days. Following this, the temperature fell by lysis, and the vital capacity gradually increased but did not attain its preoperative level. The patient was discharged on the forty-third postoperative day. On admission, the vital capacity was 4,450 cc.; on discharge 3,000 cc. (compare with chart 3).

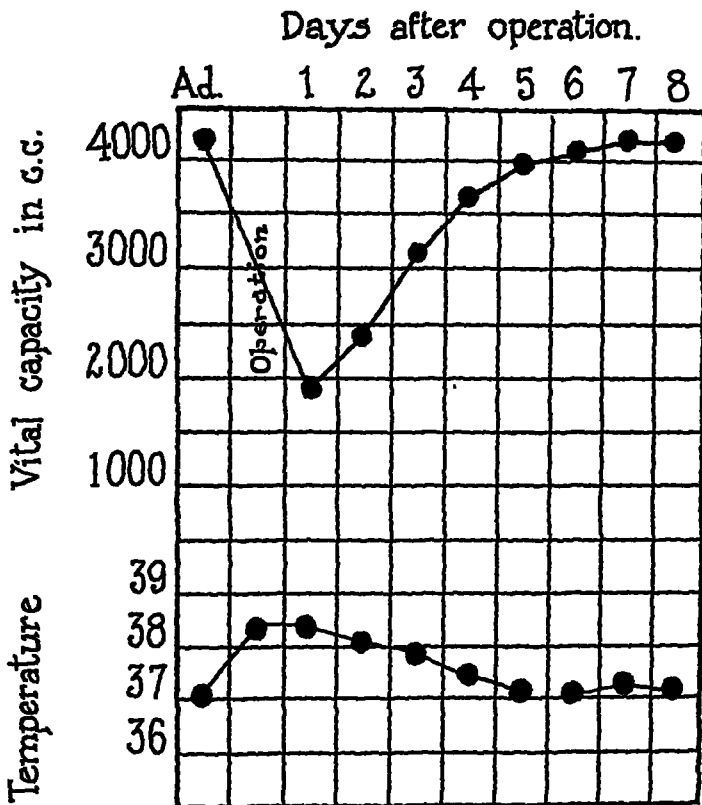


Chart 9.—Vital capacity of five patients on whom thyroidectomy was performed.

Chart 14 indicates the effect of postoperative abdominal complications on vital capacity. The patient was a well developed and well nourished man, aged 49. Following appendicectomy and drainage of an abscess under gas-oxygen-ether anesthesia, the vital capacity remained depressed and the temperature elevated. From this low level, a definite downward trend was noted on the sixth day, and rectal examination revealed a pelvic abscess. This was drained through the abdomen the following day. The vital capacity continued its downward course, and two days after the second operation, general peritonitis was present.

rise in temperature similar to that observed after the first operation. The temperature rapidly subsided, however, and the physical examination did not reveal evidence of any pulmonary complication. The vital capacity showed a normal upward trend and recovered its preoperative level on the tenth day.

Chart 13 represents the vital capacity and temperature of a youth, aged 21, operated on for acute appendicitis. There was a marked fall in the vital capacity on the first postoperative day and a rapid recovery

TABLE 7.—Operations on the Extremities

| On Admission | Days After Operation | | | | | | | |
|--------------|----------------------|-------|-------|-------|-------|-------|-------|-------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| 4,400 | 4,460 | 4,400 | 4,400 | 4,500 | 4,480 | 4,480 | 4,480 | 4,480 |
| 3,220 | 3,150 | 3,240 | 3,320 | 3,370 | 3,320 | 3,360 | 3,410 | 3,380 |
| 4,100 | 4,350 | 4,340 | 4,350 | 4,350 | 4,350 | 4,350 | 4,350 | 4,350 |
| 3,290 | 2,050 | 2,140 | 1,900 | 2,300 | 2,000 | 2,400 | 2,750 | 2,820 |
| 4,800 | 4,780 | 4,860 | 4,860 | 4,860 | 4,860 | 4,860 | 4,860 | 4,860 |
| 3,490 | 3,450 | 3,460 | 3,400 | 3,510 | 3,450 | 3,510 | 3,510 | 3,510 |
| 4,210 | 4,320 | 4,290 | 4,280 | 4,320 | 4,320 | 4,320 | 4,320 | 4,320 |
| 3,220 | 2,420 | 2,510 | 2,650 | 3,150 | 3,200 | 3,160 | 3,220 | 3,260 |
| 4,000 | 3,650 | 3,750 | 3,810 | 3,850 | 3,700 | 3,790 | 3,810 | 3,850 |
| 4,500 | 4,610 | 4,720 | 4,710 | 4,710 | 4,710 | 4,710 | 4,710 | 4,710 |
| 3,560 | 3,300 | 3,520 | 3,600 | 3,700 | 3,760 | 3,800 | 3,880 | 3,790 |
| 4,050 | 3,630 | 3,180 | 3,620 | 3,800 | 3,840 | 3,930 | 3,900 | 4,000 |
| 4,900 | 4,600 | 4,850 | 4,880 | 4,900 | 4,900 | 4,900 | 4,900 | 4,900 |
| 2,610 | 2,540 | 2,520 | 2,390 | 2,600 | 2,600 | 2,450 | 2,550 | 2,670 |
| 4,710 | 4,480 | 4,420 | 4,690 | 4,750 | 4,790 | 5,000 | 5,000 | 5,000 |
| 3,937 | 3,716 | 3,747 | 3,804 | 3,911 | 3,931 | 3,935 | 3,981 | 3,998 |
| 100% | 94% | 95% | 96% | 99% | 100% | 100% | 101% | 101% |

TABLE 8.—Thyroidectomy

| On Admission | Days After Operation | | | | | | | |
|--------------|----------------------|-------|-------|-------|-------|-------|-------|-------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| 4,790 | 2,100 | 3,400 | 3,860 | 4,140 | 4,800 | 4,620 | 4,800 | 4,900 |
| 3,200 | 1,360 | 1,680 | 2,350 | 2,800 | 2,900 | 3,120 | 3,220 | 3,220 |
| 4,500 | 1,800 | 2,090 | 3,100 | 3,560 | 4,150 | 4,500 | 4,500 | 4,500 |
| 4,400 | 910 | 1,750 | 2,840 | 3,600 | 4,420 | 4,400 | 4,400 | 4,400 |
| 4,350 | 3,450 | 3,100 | 3,640 | 4,110 | 4,220 | 4,360 | 4,390 | 4,330 |
| 4,248 | 1,924 | 2,400 | 3,158 | 3,642 | 3,998 | 4,180 | 4,280 | 4,274 |
| 100% | 45% | 57% | 74% | 89% | 94% | 98% | 101% | 101% |

which on the eighth and ninth days had not reached the preoperative level. The temperature remained elevated and on the ninth day rose still higher to 39.5 C. (103 F.). On the tenth day, a marked reduction in vital capacity occurred but no clinical evidence of a pathologic process in the chest could be found. The temperature continued upward; on the eleventh day, there was a further reduction in vital capacity and physical examination revealed bronchopneumonia. In two days, the vital capacity fell from 3,920 cc. to 610 cc. During the next twelve days, the temperature gradually subsided to normal and the vital capacity increased to 2,690 cc. On the twenty-third day, the patient complained of thoracic pain on deep inspiration; the vital capacity fell to 1,290 cc.

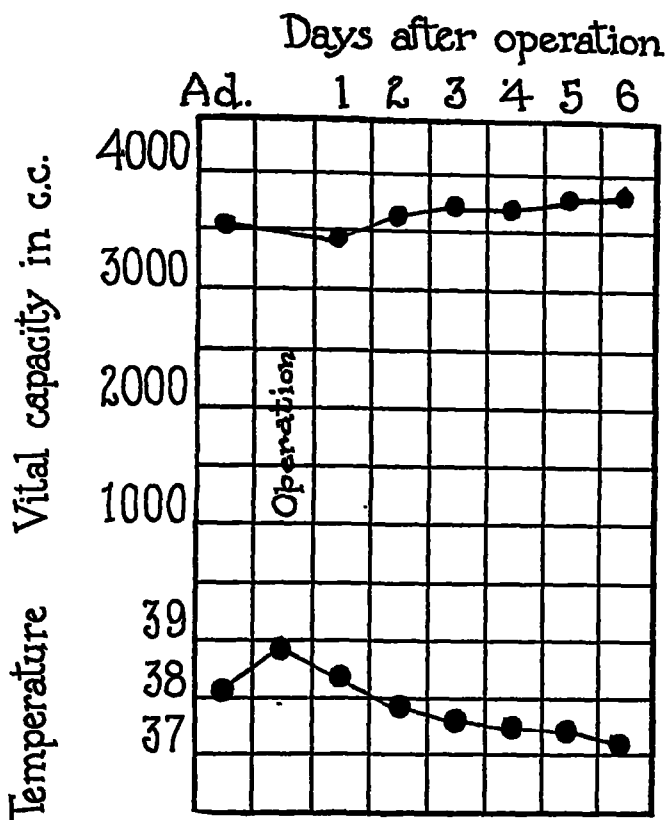


Chart 10.—Vital capacity of four patients subjected to other operations on the neck.

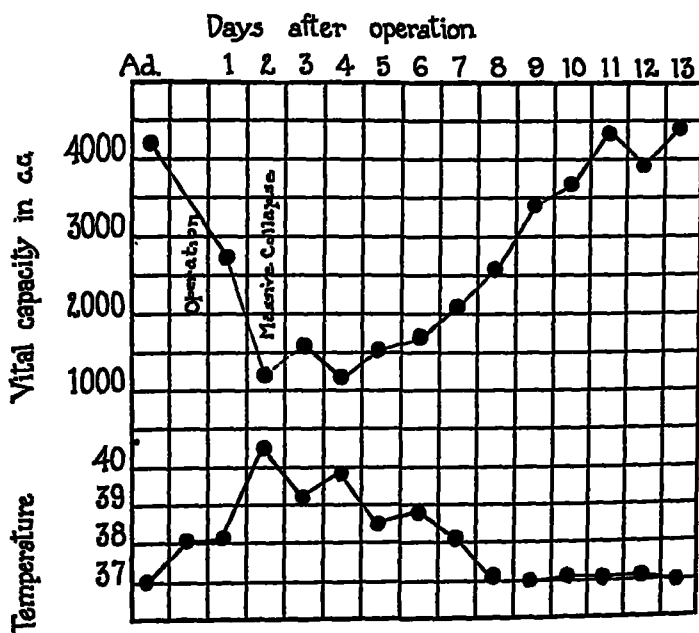


Chart 11.—Vital capacity and temperature of a patient on whom operation for unilateral hernia was followed by massive collapse of the right lung.

During the next five days, the vital capacity remained at essentially the same level and the temperature at 38 C. (100.4 F.). The patient was extremely sick; his pulse was weak and rapid; the abdomen was spastic and distended. On the sixth day after the development of general peritonitis, a definite improvement occurred in his clinical condition; the vital capacity was higher and the temperature lower. From then onward there was a gradual but steady upward trend to the vital capacity curve. The temperature returned to normal almost immediately (compare with chart 3).

Chart 15 illustrates the effect on the vital capacity of appendectomy complicated by general peritonitis. The patient was a well developed and well nourished colored man, aged 26. The preoperative vital capacity was somewhat below normal. Because of this, the subsequent decrease on the first postoperative day was less than usual. On the second day, the patient showed clinical evidence of generalized peritonitis and a further reduction in vital capacity occurred. During the next

TABLE 9.—*Other Operations on the Neck*

| On Admission | Days After Operation | | | | | |
|--------------|----------------------|-------|-------|-------|-------|-------|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| 3,610 | 3,400 | 3,850 | 3,820 | 3,900 | 4,000 | 4,020 |
| 3,620 | 3,440 | 3,510 | 3,690 | 3,720 | 3,720 | 3,720 |
| 3,880 | 3,800 | 3,420 | 3,700 | 3,640 | 3,700 | 3,700 |
| 3,720 | 3,620 | 3,750 | 3,670 | 3,620 | 3,800 | 3,840 |
| 3,582 | 3,440 | 3,632 | 3,720 | 3,720 | 3,805 | 3,820 |
| 100% | 96% | 101% | 104% | 104% | 100% | 100% |

three days, his vital capacity and clinical condition remained essentially the same. On the sixth postoperative day, a slight improvement was noted in both. Recovery was slow. He was discharged on the twenty-first day; the vital capacity was 3,200 cc. on discharge, 1,850 cc. on admission (compare with chart 3 and 14).

Chart 16 represents the vital capacity and temperature of a white man, aged 34, subjected to cystectomy and transplantation of the ureters into the rectum because of carcinoma of the bladder. The usual reduction in vital capacity occurred on the first postoperative day, accompanied by a rather marked elevation of temperature. On the third day, the vital capacity had increased slightly and the temperature had subsided to 38.2 C. (100.7 F.). On the fourth day, however, a secondary reduction in vital capacity was apparent and the temperature had again risen to 38.8 C. (101.4 F.). Examination of the patient revealed evidence of general peritonitis. The following day, there was a slight improvement in the vital capacity. This was only temporary, however, and the general trend was downward until death occurred on the thirteenth day after operation (compare with chart 5).

thyroidectomy is hard to explain. Possibly exposure of the trachea, retention of mucus, congestion and edema of the air passages may have some bearing on it. It may be that the excitement, apprehension and psychic instability characteristic of the majority of patients after thyroidectomy secondarily restrict their voluntary respiratory control.

By far the greatest reduction occurs when the operative incision is located in the upper part of the abdomen and invades the epigastric triangle. There is still a veil of mystery obscuring the accuracy of knowledge regarding the effect of upper abdominal operations. Cutler

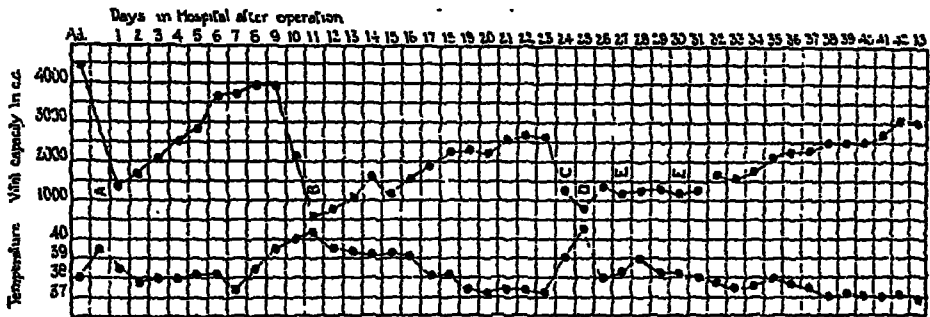


Chart 13.—Vital capacity and temperature curves of a patient on whom appendicectomy was performed; bronchopneumonia and pleurisy with effusion followed. *A* indicates operation; *B*, bronchopneumonia; *C*, pain on effusion; *D*, pleurisy with effusion; *E*, thoracentesis.

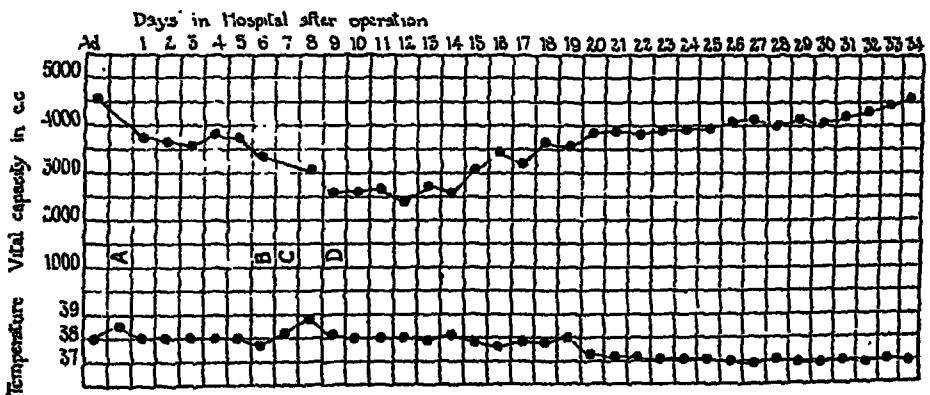


Chart 14.—Vital capacity and temperature curves of a patient on whom appendicectomy was performed; a residual pelvic abscess was drained and general peritonitis developed. *A* indicated operation; *B*, pelvic abscess; *C*, drainage and *D*, general peritonitis.

and Hunt¹⁷ found that postoperative pulmonary complications occur in 8 per cent of epigastric operations, 4 per cent of laparotomies and 2 per cent of all operations. They attributed this to greater mobility of the field during operation and the consequent greater freedom with which multiple small emboli may be dislodged. Subsequent to epigastric

17. Cutler and Hunt (footnote 9 and 10).

No other postoperative complications developed, and consequently no curves are available for comparison with normal curves following operations on the upper part of the abdomen, extremities, neck or rectum.

COMMENT

Since this work was started, two articles have appeared on vital capacity before and after operation. The curves presented in this paper compare favorably with those of Churchill and McNeil¹⁵ and Head.¹⁶

It is evident from an analysis of the charts and tables that abdominal operations produce a tremendous immediate decrease in vital capacity followed by a gradual return to normal. There is an apparent similarity in the curves for each type of operative incision.

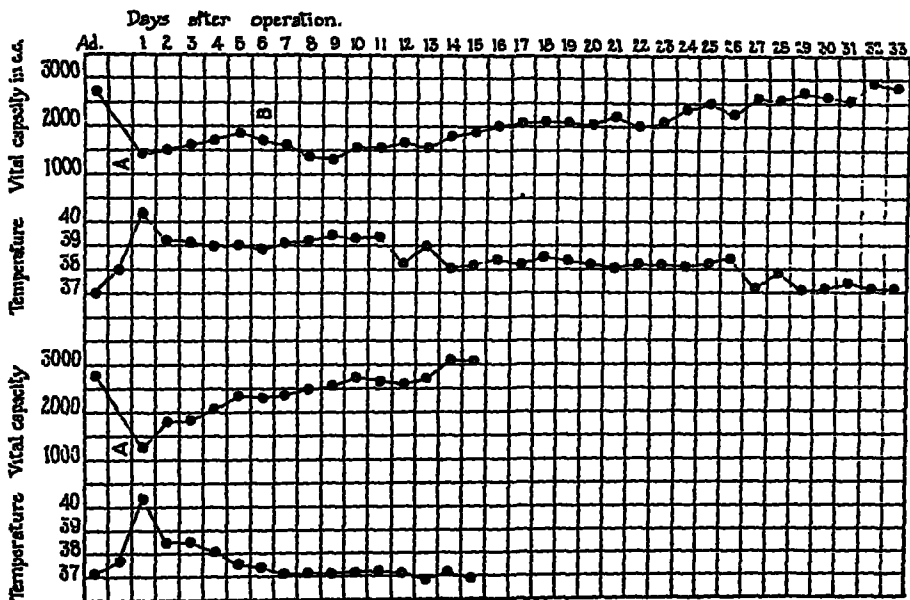


Chart 12.—Vital capacity and temperature curves of a patient operated on for right inguinal hernia; postoperative bronchopneumonia followed; an operation for left femoral hernia was attended by a normal convalescence. *A* indicated operation; *B*, pneumonia.

Partial removal of the thyroid gland likewise entails an immediate and pronounced fall in the vital capacity followed by a rapid recovery. All other operations on the neck and those on the extremities and rectum have no effect on the vital capacity. The reason is obvious; the muscles of respiration are not involved in the operative incision. Why the vital capacity should be so profoundly, though temporarily, affected by

15. Churchill, E. D., and McNeil, D.: The Reduction in Vital Capacity Following Operation, *Surg. Gynec. Obst.* 44:483, 1927.

16. Head, J. R.: The Effect of Operation Upon the Vital Capacity, *Boston M. & S. J.* 197:83, 1927.

ASCARIASIS OF THE GALLBLADDER

LITERATURE AND CASE REPORT

CHARLES BRUCE MORTON, M.D.

Assistant Professor of Surgery and Gynecology, in the University of Virginia
UNIVERSITY, VA.

Ascariasis is not usually grouped among the diseases requiring surgical intervention, and its presence in what may be called a surgical form is probably seldom diagnosed prior to operation. Ascariasis of the gallbladder is especially unusual, if one may judge by the infrequency with which it has been recorded in the literature. The finding of an ascarid in the gallbladder of a woman on whom I recently performed an operation for cholecystitis suggested this study.

LITERATURE

The literature contains numerous references to cases in which ascarids were found in other unusual sites: the urinary passages, the appendix, the pancreatic duct, the common bile duct and the hepatic ducts. Ascarids in these locations were credited with causing many types of symptoms, chiefly those of obstruction and inflammation, presenting, however, few if any pathognomonic peculiarities. DaCosta¹ in his textbook on surgery, does not mention ascariasis among the diseases of the gallbladder. Only three direct references to the presence of parasitic worms in the gallbladder were found in the literature. Of the many other articles indexed under "ascariasis," "gallbladder," and other heads, only the more likely were investigated. In this group, only five additional articles were found in which ascariasis of the gallbladder was mentioned.

In 1765, Lorry,² quoted by Aviles, recorded the first case found in the literature. He cited the case of an insane patient in whose gallbladder three ascarids were found at necropsy. This patient vomited a worm prior to death and died in convulsions, presumably caused by the presence of the parasites in the gallbladder. Aviles³ recorded a case of ascariasis of the gallbladder encountered at operation and summarized

1. DaCosta, J. C.: *Modern Surgery*, ed. 9, Philadelphia, W. B. Saunders Company, 1925.

2. Lorry, A. C.: *De melancholia et morbis melancholicis* 16:339; 8:429, Lutetiae Parisiorum. P. G. Cavelier, 1765.

3. Aviles, J.: *The Rôle of Ascariasis in Gallbladder Disease*, Surg. Gynec. Obst. 27:459, 1918.

operations, there is a more complete and prolonged splinting of the abdomen and lower part of the thorax, with the result that the respiratory movements are more grossly impaired over a longer period of time than after operations on any other part of the body. May not this pulmonary embarrassment and comparative immobility play some part in the more frequent occurrence of postoperative complications follow-

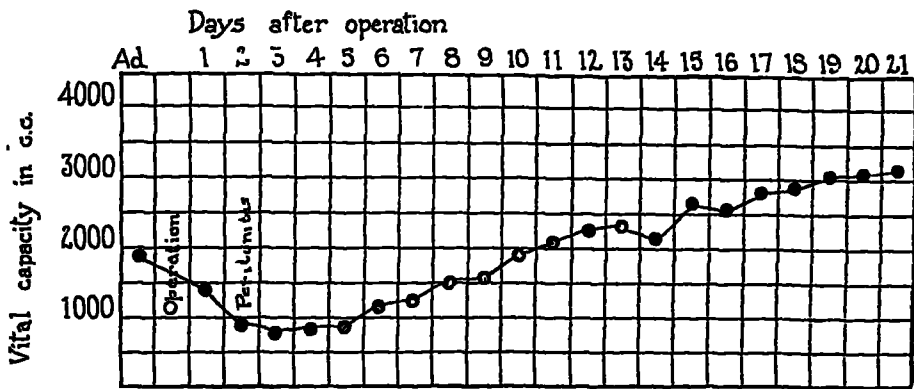


Chart 15.—Vital capacity of a patient subjected to appendectomy for ruptured appendicitis and general peritonitis.

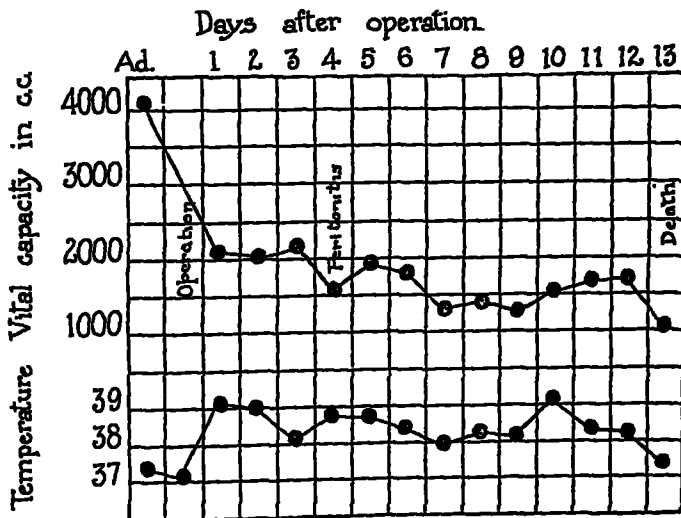


Chart 16.—Vital capacity of a patient subjected to cystectomy and transplantation of the ureters; general peritonitis developed and death ensued.

ing upper abdominal incisions? Karsner and Ash¹⁸ showed experimentally that a partially atelectatic lung offers a more fertile soil for the reception of emboli than one which is normally aerated. The sequence of events seems logical. Most upper abdominal incisions are placed to the right of the midline; consequently, expansion of the lower lobe of

18. Karsner, H. T., and Ash, J. E.: Studies in Infarction: II. Experimental Bland Infarction of the Lung. *J. M. Research* 22:205, 1912-1913.

worms as short as $1\frac{1}{4}$ inches (3.1 cm.) in length in the bile ducts. Stiles¹¹ said: "The eggs of the ascaris will not hatch as long as they are in the human body. They must pass out and there undergo their changes. The young worm is developed inside the egg, the egg is then swallowed, hatches out in the stomach, crawls through the wall of the stomach, gets into the circulation, goes to the heart and lungs, up the trachea, down through the stomach to the small intestine, and there develops further." Others differ with this opinion and believe that ova which contain embryos and which are still surrounded with the mulberry envelop will develop into roundworms in the human intestine.

The cases of ascariasis of the gallbladder were not recorded in anything approaching a uniform manner. There are, however, certain similarities in all of them which form a rather clearcut composite picture.

The data in the two cases quoted by Devaine were very meager and the brief facts of Lorry's case have already been quoted. The cases of ascariasis reported by Aviles, Tyau, Eberle, and Butt and the case of taeniasis reported by Benedict were complete enough for instructive study, and I shall summarize them.

REPORT OF CASES

AVILES' CASE.—A woman, aged 38, had suffered with attacks of pain in the upper part of the right side of the abdomen for twenty-six years. Attacks had been increasingly severe for the last year. She had occasionally vomited roundworms. For six days before admission to the hospital she suffered continuous pain, which radiated to the right shoulder blade and was accompanied by slight icterus and moderate fever. The diagnosis of cholecystitis with probable cholelithiasis was made, and the abdomen was explored. An *Ascaris lumbricoides* 8 inches (20.32 cm.) in length was found in the gallbladder obstructing the cystic duct. The worm was removed, and a cholecystostomy was performed. Anthelmintics were administered during the postoperative convalescence.

TYAUS' CASE.—A man, age not mentioned, had suffered for three months with epigastric pain which radiated to the liver region but not to the shoulder. A mass suspected of being the gallbladder was palpable. Ova of *Ascaris lumbricoides* and *Trichuris trichiura* were found in the stools. Santonin was administered and eighteen roundworms evacuated, but the symptoms were not relieved. Five days later, the patient died. Necropsy disclosed nine roundworms occluding the cystic duct. There were multiple abscesses of the liver and several roundworms in the hepatic ducts. Ova were found in the gallbladder, the biliary ducts and the liver itself.

EBERLES' CASE.—A boy, aged 9 years, had been treated with santonin for intestinal parasites. Five months later, he complained of pain in the upper part of the right side of the abdomen, and there were symptoms of jaundice. The abdomen was explored for gallbladder disease, and a living roundworm was found in the gallbladder. Three more worms, all alive, were found in the hepatic duct.

BUTT'S CASE.—A woman, aged 30, mother of three children, had had six attacks of severe pain in the upper part of the right side of the abdomen during

11. Stiles, C. W.: Personal communication to Butts.

the literature. He quoted two other authors, Bonfils⁴ (1858) and Devaine⁵ (1860), who had recorded "a few cases." Bonfils quoted Lorry, Devaine quoted Lorry's case and two other cases which were attributed to Heaviside and Bloch.

In 1922, Butt⁶ added a case of his own to the literature and quoted Tyau⁷ (1920) and Eberle⁸ (1920), who reported two more cases. Up to the time of this writing no other cases of ascariasis of the gallbladder were found in the literature. However, Benedict,⁹ in 1926, reported a case in which *Taenia saginata* was found in the gallbladder. Because of its similarity to the cases in which *Ascaris lumbricoides* was present in the gallbladder, it is probably of more than passing interest.

That animals as well as man may harbor ascarids in the gallbladder was ascertained from Schlotthauer.¹⁰ He, dealing with numerous laboratory and domestic animals, stated that he had occasionally encountered ascarids in the gallbladder of swine. They were apparently an incidental observation, and no symptoms or pathologic changes were ascribed to their presence.

Aviles called attention to the wide and almost universal geographic distribution of *Ascaris lumbricoides*, and said that the pathogenicity of the parasite depended on three characteristics. The first was a poisonous material found in extracts of the worm; the second was the carrying of infection by the motile and migratory traits of the ascarid, and the third was mechanical, the obstruction in a hollow viscus sometimes caused by a parasite or group of parasites. The last two characteristics are of primary importance in considering ascariasis of the gallbladder.

Another important consideration is the life cycle of the parasite. Knowledge of this is necessary in attempting to determine whether an ascarid found in the gallbladder has come there as an ovum and subsequently hatched, or whether its presence there is the result of migration of a worm from the intestine. Ova of *Ascaris lumbricoides* were found in the gallbladder and bile ducts by Tyau, and he also found

4. Bonfils, E. A.: Des lésions et des phénomènes pathologiques déterminés par la présence des vers ascarides lombricoïdes dans les canaux biliaires, p. 28. Paris, Rignoux, 1858; reprinted from Arch. gén. de med., Paris, 1858.

5. Devaine, C.: Traité des entozoaires et des maladies vermineuses de l'homme et des animaux domestiques, Paris, 1860, p. 156.

6. Butt, A. P.: Round Worm (*Ascaris lumbricoides*) in Gallbladder, Surg. Gynec. Obst. 35:215, 1922.

7. Tyau, E. S.: Pathogenicity of *Ascaris lumbricoides*; Report of Cases. M. J. China, 6:21, 1920; abstr., J. A. M. A. 75:135 (July 3) 1920.

8. Eberle, D.: Ascarids in the Liver and Pancreas, Schweiz. med. Wchnschr. 50:1110, 1920; abstr., J. A. M. A. 76:344 (Jan. 22) 1921.

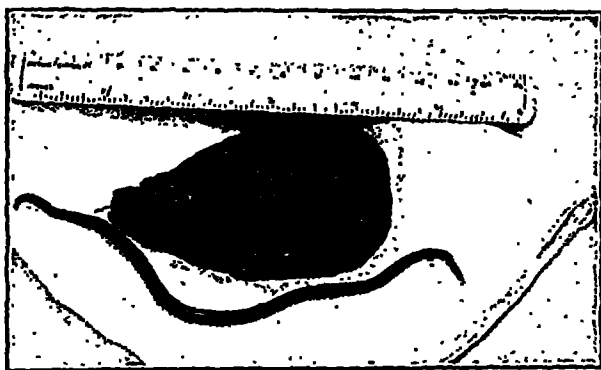
9. Benedict, E. B.: *Taenia Saginata* in the Gallbladder, J. A. M. A. 87:1917 (Dec. 4) 1926.

10. Schlotthauer, C. S.: Personal communication to the author.

following intravenous injections of dye (tetra-iodo-phenolphthalein) failed to show any trace of a shadow of the gallbladder. Subacute cholecystitis with probable cholelithiasis was the diagnosis made, and an operation was advised.

On Nov. 17, 1927, I made a high incision through the right rectus muscle and explored the abdomen. The pelvic organs, appendix, kidneys, stomach and duodenum apparently were normal. The gallbladder was surrounded with recent adhesions to adjacent structures and was distended to a diameter of about 8 cm. at the fundus. Stones were not palpated, and the gallbladder did not empty under pressure. The walls were thickened. The common bile duct was not enlarged, and stones were not palpated in it. The gallbladder was removed from below outward, and the abdomen closed without drainage.

Pathologic examination of the gallbladder disclosed thickening and subacute inflammation of the walls. The mucosa showed some cholesterol deposits. The bile was of about normal consistency. In the gallbladder was discovered a living, actively motile roundworm, *Ascaris lumbricoides*, which measured 17.5 cm. in length (fig. 1).



Ascarid and gallbladder removed from patient.

Postoperative convalescence was quite uneventful, and the patient was allowed to go home on Dec. 4, 1927, eighteen days after her operation. Anthelmintics were advised to rid her of any parasites remaining in the intestinal tract.

Following the unusual and unexpected operative observation, the patient was carefully questioned concerning her previous history. She again denied any former attacks of pain in the gallbladder region, and said that she did not know that she harbored intestinal parasites until the day before operation. On that day she was nauseated and vomited an *Ascaris lumbricoides* 15 cm. in length.

COMMENT

The problem of how a parasitic worm may have arrived in the gallbladder is one difficult to solve. One must assume either the hatching of an ovum in the gallbladder or the migration from the intestine of a worm sufficiently small to pass through the cystic duct. In Benedict's case, a taenia 10 feet (304.8 cm.) long was found in the gallbladder. How long this parasite had been in the gallbladder is not easy to determine, although it is improbable if not entirely impossible to suppose that it could have passed through the cystic duct while measuring anything approximating 10 feet in length.

I made a tabulation of the cases of ascariasis found in the literature and included my own case and that of Benedict, in which the parasite was not an ascarid but *Taenia saginata*. The incidence in the two sexes is about equal, and the age limits vary between 9 and 74 years. There are two factors, however, which are constant in every case; the history of intestinal infestation with parasites and symptoms referable to the gallbladder.

These two constant features of the cases do not assure the diagnosis, but when elicited they should at least lead one to bear in mind the possibility of ascariasis of the gallbladder.

The treatment for ascariasis of the gallbladder is the same as that for inflammation or obstruction of the organ due to other causes. As suggested by Butt, cholecystectomy is probably the operation of choice. Anthelmintics are indicated as a prophylactic measure in all persons with intestinal parasites and as a postoperative measure in ascariasis of the gallbladder to rid the patient of any remaining parasites.

SUMMARY

The literature was searched for cases of ascariasis of the gallbladder. Seven cases were found and five have been briefly summarized. A case of taeniasis of the gallbladder was found and also summarized. It was similar in many respects to the cases of ascariasis. All cases had been diagnosed only after operation or necropsy.

A case of ascariasis of the gallbladder which I encountered has been described, and the condition discussed in relation to its etiology, diagnosis and treatment. It was pointed out that the disease is rare and difficult to diagnose. Furthermore, the treatment is surgical and cholecystectomy is probably the operation of choice. Anthelmintics are indicated for prophylactic use and postoperatively. The history of ascariasis in a patient with signs of cholecystic disease should always suggest the possibility of ascariasis of the gallbladder.

Probably the preoperative diagnosis of ascariasis of the gallbladder will never be made with any great degree of certainty. In the first place, it is obviously a rather rare condition and one which would hardly be thought of unless one were to bear it in mind in all cases of cholecystic disease. In the second place, the symptoms of the disease do not differ in general from those of the commoner varieties of inflammation and obstruction of the gallbladder and cystic duct.

Outline of Cases Found in Literature and of My Own Case

| Case Reported by | Sex | Age | Past History | | Complaint | Pre-operative Diagnosis | Observations at Operation | Results |
|--|-----|--------------------------------------|--|-------------------------------|-----------------------------------|--|---|---|
| | | | Ascariasis | Gallbladder | | | | |
| Heavyside and Bioch, quoted by Devaine, 1800 | | 2 cases, were not recorded in detail | | | | | | |
| Lorry, 1765... | .. | .. | Vomited an ascarid | | Convulsions | | | Necropsy: three ascarids in gallbladder |
| Aviles, 1918... | F | 38 | Vomited ascarids occasionally | Periodic attacks for 26 years | Gallbladder colic for 6 days | Cholecystitis; probable cholelithiasis | Ascarid 8 inches long in gallbladder | Cholecystostomy |
| Tyau, 1920.... | M | .. | Ova found in stools | Pains for 3 months | Pain and mass in gallbladder area | | | Necropsy: nine ascarids in cystic duct |
| Eberle, 1920... | M | 9 | Treated for ascariasis 5 months previously | Pain and jaundice | Pain and jaundice | Cholecystitis | Ascarid in gallbladder | Cholecystostomy presumably |
| Butt, 1922..... | F | 30 | Frequently passed ascarids in stools | Periodic pain for 2 years | Gallbladder colic for 6 days | Cholecystitis; probable cholelithiasis | Ascarid 6 inches long in gallbladder | Gallbladder closed without drainage |
| Benedict, 1926 | M | 74 | Known to have taenia 2 years; raw beef eaten 50 years before | Several attacks previously | Gallbladder colic for few hours | Acute cholecystitis | Taenia 10 ft. 2 in. long found in gallbladder | Cholecystostomy |
| Morton, 1928.. | F | 45 | None except vomited ascarid day before operation | None | Gallbladder pains for 5 weeks | Cholecystitis; probable cholelithiasis | Ascarid 17.5 cm. long found in gallbladder | Cholecystectomy |

The case reported herewith illustrates the point. The history and physical observations were similar to those in numberless other cases of ordinary cholecystic disease. The laboratory and cholecystographic data were equally commonplace. The diagnosis of cholecystitis with probable cholelithiasis seemed obvious.

There was, however, one fact not taken into consideration in making the diagnosis. That was the vomiting of the ascarid the day before operation, ignored as not important at the time and yet in the light of subsequent observations it proved to be one of the most significant features of the case.

The ureters are located and severed between small artery forceps as near to the bladder as possible. The distal stump is cauterized with phenol and ligated. The proximal end of the ureter is liberated for 7.5 or 10 cm. by slitting the peritoneum over it. Ureteral catheters, provided with rubber cuffs to prevent slipping, are inserted into the ureter. A strong linen thread is passed twice around the ureter and cuff and tied tightly with a double or surgeon's knot. A similar suture is then tied around the ureter below the incision to prevent infection ascending the ureter from the bowel. Urine usually begins to escape from the catheters at once.

To avoid too much narrowing, one incision should be higher in the bowel than the other. The incision should begin near the mesenteric edge and extend downward and obliquely toward the antemesenteric border to avoid as many of the large vessels as possible. It should be about 3.8 cm. in length, and through the peritoneum and muscle, thus permitting the mucosa to pouch out partially. A small stab wound is made in the mucosa between traction sutures. A little of the gauze already inserted in the rectum is picked up with mosquito forceps, and to this the end of the cathéter is attached. After both of the catheters are attached to the gauze, the gauze is gradually withdrawn from the rectum and in so doing the ureteral ends are drawn into the openings in the mucosa. The catheters must be marked to indicate the right and left kidney. After the ureter is drawn past the ligature, the free ends of the two traction loops are tied across the ureter to close the opening partially. These traction loops, inserted before the mucosal puncture, are important in handling the intestine.

[ED. NOTE.—Coffey's method of ureteral transplantation is, at the present time, accepted by most urologists as the one giving the most satisfactory functional results. Not all urologists agree as to the indications for ureteral transplantation. Hinman²⁷ believes in transplanting the ureters into the bowel in a small group of cases. Usually this method is employed now only as a last resort, but if freed from some of its dangers, it could be applied to a larger number of cases. Hinman believes that a surgical victory over this defect must include restoration of natural relationships. To insure satisfactory renal function, a first stage preparatory nephrostomy should be performed; this is followed subsequently by ureteral transplantation.]

Marion²⁸ states that ureteral transplantation is of doubtful value. If it is performed, it is necessary to be ready to operate on the corresponding kidney in case of complications. In some cases, instead of

27. Hinman, Frank: 'The Indication of Nephrostomy Preliminary to Uretero-rectoneostomy, J. A. M. A. 86:921 (March 27) 1926.

28. Marion, M.: Suite de la discussion sur les implantations urétérales, J. d'urol. méd. et chir. 20:58, 1925.

A REVIEW OF UROLOGIC SURGERY

ALBERT J. SCHOLL, M.D.
LOS ANGELES

E. STARR JUDD, M.D.
ROCHESTER, MINN.

LINWOOD D. KEYSER, M.D.
ROANOKE, VA.

GORDON S. FOULDS, M.D.
TORONTO

JEAN VERBRUGGE, M.D.
ANTWERP, BELGIUM

AND
ADOLPH A. KUTZMANN, M.D.
LOS ANGELES

(Continued from page 178)

URETER

Transplantation.—Peterson²⁵ believes that the extraperitoneal route is more desirable than the intra-abdominal in the transplantation of the ureters into the bowel. Even with the most skilful care, the wound may become infected, and tight approximation of the suture line is difficult. If urine or feces escape around the opening through the mucosa, the patient usually succumbs, unless the operation has been performed extraperitoneally. Technically, it is not more difficult since the ureters are readily exposed and easily transplanted.

Peterson reports several cases of incurable vesicovaginal fistula in which transplantation of the ureters was carried out in order to secure sphincteric urinary control. He does not expose the patient to the additional risk of transplanting both ureters at the same operation.

In Coffey's²⁶ earlier papers, he advises the insertion of a small rubber tube into the ureter before transplantation. The greatest trouble in ureteral transplants, especially in animal experimentation, is infection emanating from the opening in the intestine. At present, Coffey uses the following technic: The bowel is cleansed with castor oil and enemas before operation. The abdomen is opened low near the median line, and the sigmoid is pulled down into the field of operation. A sigmoidoscope is inserted into the rectum, and the lower part of the bowel is flushed by a pointed cannula inserted through the wall of the sigmoid. The rectum is then packed full of dry gauze, and the sigmoidoscope is removed.

25. Peterson, Reuben: Transplantation of the Ureters into Bowel to Secure Sphincteric Urinary Control in Incurable Vesicovaginal Fistula, *Am. J. Obst. & Gynec.* 14:492, 1927.

26. Coffey, R. C.: Completed Aseptic Technique for Implantation of Ureter into Large Bowel, *Surg. Gynec. & Obst.* 45:816, 1927.

in man. The fundamental requisite is a sustained tonic contraction of the musculature of the bladder as it actively resists distention. Atonic bladders never regurgitate; postmortem experiments are futile. Moreover, as Graves has shown, there are no intrinsic anatomic differences, such as have been claimed, between the ureterovesical relationship of the laboratory animal and of the human being.

In general, then, it may be stated that there are two groups of bladders so far as reaction to distention is concerned. One group, marked by an active state of muscle tone, resists distention, and in these tracings of intravesical pressure show a constant, relatively rapid, rise of tension as filling proceeds. Such bladders will regurgitate when the normal outlet is obstructed in a large percentage of cases, as he has demonstrated in a long series of observations on animals. The other group, in which tone is relatively lacking, consists of bladders that offer feeble or no resistance to the force of distention. These bladders fall away from the distending fluid, and there is no appreciable sustained rise in intravesical pressure until the end-stage of filling is reached, when, as has been said, a purely mechanical tension is produced because the sac can hold no more. In this passive type of bladder, regurgitation does not occur.

As Graves was dealing with fundamental reactions of smooth muscle, it seemed reasonable to expect in starting this particular investigation that the bladder of man, in its behavior during distention, would fall into one or the other of these groups and so give further evidence of support or denial of the clinical theory of regurgitation. To answer this phase of the question, he has made use of an instrument which has just been completed and which makes it possible to record accurately the development of intravesical pressure during filling of the bladder. The instrument consists of a reservoir from which the bladder may be filled with a definite volume and rate of speed through the action of a small piston pump. There is also a mercury manometer which communicates with the recording device and which is in open communication with the cavity of the bladder throughout the period of filling. Geared to the pump is a small kymograph which provides the permanent record of the manometer as it registers the changes in intravesical tension.

Thus far, however, he has noted only one case, that of a long-standing stricture with infection, which would not be classified beyond question with the active tonic group of bladders that he has described experimentally and that permitted reflux in so large a percentage of cases. Only the atonic bladder of disease of the spinal cord was of the passive type. The curves for the human being are similar to those for animals; from this analogy, Graves claims support for the probability of regurgitation in the bladder of man.

reimplantation, primary or secondary nephrectomy may be desirable. He believes that in most cases the kidney of the ureter that has been transplanted becomes dilated and gradually atrophies. Legueu, in discussing Marion's statements, states that he has noted only one favorable case of transplantation reported in the literature, that of a patient who, seventeen years after transplantation of the ureter, still had a well functioning kidney.

Papin²⁹ states that in his experience, ureteral transplantation is more satisfactory than simple nephrostomy. Isolation of the ureter from its normal connections disturbs its functioning power; it becomes atonic and dilated and contracts more slowly and less frequently. All surgical procedures on the ureter cause infection; the resulting dilatation of the ureter is responsible for most ascending infections. Papin gives three methods of transplanting the ureter: transplantation to the skin, transplantation into the urethra and transplantation into the intestine. He believes that the transplantation to the skin is the safest of the three methods.

Smitten³⁰ compiled a series of 318 cases of implantation of the ureters into the intestine with the following results: fistula of the bladder, 156 cases, with death in 34 (21.8 per cent); anomalous conditions, 58 cases, with death in 18 (31 per cent); malignant tumors, 98 cases, with death in 61 (63 per cent), and inflammatory processes, 4 cases, with death in 3 (75 per cent). Of the total number of patients, 116 died and 200 recovered; in 2 cases the result was not known. Thirty patients died from peritonitis, 21 from urinary infection, 5 from pneumonia and 3 from tuberculosis. The late results, from six months to ten years, were known in 71 cases. In 6 of these death was caused by renal insufficiency, in 3 by recurrence of the original condition, and in 2, by intercurrent disease.

In many cases, the time consumed and the difficulty of the operation do not justify the attempt to preserve renal tissue. The ureter is often already dilated and infected and the corresponding kidney is only slightly infected. On the other hand, in certain cases, such as exstrophy of the bladder in young patients, ureteral transplantation is unquestionably a life-saving procedure.

Regurgitation.—Graves,³¹ in continuing his studies on regurgitation from the bladder into the ureters under normal conditions at the ureterovesical juncture, investigated the pressure curve of the bladder

29. Papin, M.: La dérivation haute des urines, *Presse méd.* 2:1412, 1925.

30. Smitten, A. T.: Ueber die Einpflanzung der Ureteren in den Darm, *abstr. Ztschr. f. urol. Chir.* 19:219, 1926.

31. Graves, R. C.: IV. Studies on the Ureter and Bladder with Especial Reference to Regurgitation of Vesical Contents; Bladder Pressure-Curve in Human, *J. Urol.* 18:321, 1927.

is always dangerous and should be performed only when other tests of renal function give good results.

Suitable preoperative treatment usually results in reestablishing renal function and in rendering the patient fit for prostatectomy. In some cases, the function of the kidney cannot be improved sufficiently by catheter drainage; in these, the two-stage operation should be performed.

Wildbolz believes that the perineal operation puts much less strain on the heart and lungs and causes less shock than the suprapubic. He finds that suprapubic prostatectomy is usually followed by an increase in the blood urea, lasting for several days, but after a perineal operation there is practically no such increase. The perineal operation does not cause nearly so much bleeding, and the perineal wound does not hinder respiration or expectoration. Furthermore, the perineal operation is not followed by necrosis of the tissues, and the wound is so well drained that there is only a slight amount of absorption which may increase the blood urea.

Wildbolz uses the same incision in performing perineal prostatectomy as that employed by Zuckerkandl, Albarran and Proust, with a slight modification used also by Young. The central tendon of the perineum is exposed and cleaned. A small transverse incision is made in it close to the bulb, and the recto-urethralis muscle is exposed. This is divided close to the urethra, and the prostate is exposed by blunt dissection. On the anterior wall of the wound are the bulb and transversus perinei muscle, and on the posterior side lies the rectum. The prostate is pressed down toward the perineum by a metal catheter introduced into the urethra. It is covered by the fascia of Dénouvillier. This fascia is divided transversely just above the apex of the gland and is pushed backward, exposing the posterior portion of the capsule in the wound. Wildbolz makes a vertical incision in the median line, commencing at least 1 cm. above the apex, which involves only the capsule of the prostate and does not penetrate to the urethra, and which enables one to distinguish between capsule and adenomatous masses. Both lobes of the prostate are enucleated as far as possible. The prostatic urethra is divided transversely just at the lower end of the adenomatous mass, the upper end still being left in connection with the neck of the bladder. Young's retractor is introduced through the prostatic urethra into the bladder, and the upper end of the urethra is divided close to the neck of the bladder, with any adhesions still existing between the adenoma and the capsule of the gland. The bladder is washed out to remove blood clots.

Four sutures are placed through the neck of the bladder, and afterward through the stump of the urethra at the apex of the gland. They unite the neck of the bladder to the urethra inside the prostatic cavity. Thus this procedure restores normal anatomic conditions as far as possi-

PROSTATE

Hypertrophy.—Troell³² reports his results in a series of 93 cases in which prostatectomy was performed, with 5.4 per cent primary mortality (82 cases of benign hypertrophy of the prostate with 4.9 per cent mortality and 11 cases of prostatic carcinoma with 9 per cent mortality). Troell accentuates the need for preoperative treatment, especially drainage of the bladder.

Four and three-tenths per cent of the patients had epididymitis; the occurrence of this condition can be limited by a frequent change of the urethral catheter both before and after operation. In the cases of carcinoma, permanent results following prostatectomy were not good; in some cases, recurrence and metastasis occurred six months after operation. Troell believes that metastasis to bone may be favorably influenced by repeated treatments with the roentgen rays.

Wildbolz³³ gives the following indications for prostatectomy: (1) permanent retention of a considerable quantity of urine in the bladder (from 150 to 200 cc. or more); (2) frequent attacks of complete retention; (3) long-standing infection of the bladder, and (+) severe repeated hemorrhage from the hypertrophied prostate.

He does not perform prostatectomy as a prophylactic measure. It is never a harmless procedure and is justified only when the patient is in real danger from disease. Wildbolz considers the water test one of the most important of all the tests for renal function. Suter of Basle refuses to perform an operation unless the urine concentrates to a specific gravity of at least 1.017. Lehmann considers 1.018 and Rubritius 1.015 to be the minimum. Wildbolz shows that these figures are unnecessarily high, as twenty-six of his patients recovered in spite of a much lower concentration of the urine. In eighteen, it was from 1.011 to 1.014; in seven, it was 1.010, and in one 1.009.

Negro and Colombet of Marion's Clinic state that operation should not be performed unless at least 42 per cent of phenolsulphonphthalein is eliminated in the first hour. Blanc considers 55 per cent as a minimum. The majority of Wildbolz's patients eliminated more than 30 per cent of phenolsulphonphthalein in the first hour, but thirteen eliminated from only 20 to 30 per cent and ten less than 20 per cent.

The observations of Wildbolz and other investigators show that prostatectomy will be followed by uremia if the urea of the blood is more than 100 mg. per hundred cubic centimeters, and probably so if it is over 80 mg. When the blood contains from 50 to 80 mg., the operation

32. Troell, Abraham: Prostatectomy: Some Remarks About Indications, Technique and Results, *Acta chir. Scandinav.* 62:133, 1927.

33. Wildbolz, Hans.: Indication and Execution of Prostatectomy, *Proc. Roy. Soc. Med., Sect. Urol.* 20:50, 1927.

these causes of death. Two types of cases present the greatest hazards in prostatectomy: those in which prolonged urinary retention has resulted in marked renal insufficiency, and acute uremia and death are readily precipitated by immediate prostatectomy; and those in which the urinary tract is free from infection, only a few ounces of urine are retained as the result of prostatic obstruction, and there is little or no impairment of renal function, a type of case in which general sepsis is likely to be precipitated by immediate prostatectomy. Experience has taught that in the first type the patient may recover from actual or potential uremia, that renal efficiency may be restored or approach normal, and that the cardiovascular renal reserve may be increased by a period of careful and adequate preoperative treatment. In the second type of case, the patient may likewise be provided with immunity to infection by the same means.

Recent investigation of the relationship of preliminary treatment to mortality following prostatectomy has definitely established the necessity of preliminary treatment in all cases.

Hunt believes that in 75 per cent of cases prostatectomy can safely be performed by the one-stage visualized operation, which permits the application of the general principles of surgery, that is, exposure, accuracy of conduct and complete hemostasis. He emphasizes the importance of avoiding anesthesia by inhalation, and of using the various forms of local anesthesia. The advantages of the one-stage over the two-stage operation are also dealt with, and the operation is illustrated.

The discussion of mortality in this paper is based on a five year period, during which time suprapubic prostatectomy was performed on 995 patients at the Mayo Clinic.

This series has been carefully reviewed with regard to the mortality rate, subsequent course and ultimate function. In several series of cases of 100 each, there were no deaths. The mortality rate by years, however, has varied from 6.4 per cent in one year to 2.4 per cent in 1925, with an average rate of 4.2 per cent for the five year period. In this connection, it should be stated that previous to January, 1925, preoperative preparation was carried out in only about 75 per cent of the cases. The remaining 25 per cent of the patients were in excellent general condition and were operated on without preoperative preparation. The effect of preoperative preparation in all cases after January, 1925, became apparent immediately.

The one-stage operation was performed in 783 cases (78.6 per cent) of the series with 34 deaths, a mortality rate of 4.3 per cent. In 212 cases, the two-stage operation was performed with 8 deaths, a mortality rate of 3.7 per cent. This is in contrast with a previous report on an earlier series of cases in which the mortality rate of the two-stage operation was one and a half times as high as that for the one-stage operation.

ble. Before the sutures are tied, the metal catheter is replaced by a silk one which is retained for twelve or fourteen days after operation. A drainage tube is placed in the opening of the prostatic capsule, which is partially closed by means of a single suture. Packing is not inserted. The superficial part of the wound is brought together by a few sutures. As a rule, the wound heals by primary intention. The perineal drainage tube is removed three or four days after operation, and the fistula heals so quickly that the catheter can be removed in from ten to fourteen days. The patient is then able to pass urine normally through the urethra.

The main points in which this method differs from other perineal operations are: (1) complete resection of the part of the prostatic urethra encircled by the adenoma, (2) suture of the neck of the bladder to the urethral stump, and (3) suture of the incised prostatic capsule.

This method of prostatectomy causes only slight injury to the tissue. Little blood is lost, and serious postoperative hemorrhage rarely occurs. Infection rarely follows perineal prostatectomy, the wound is smooth, there are no cavities or flaps of necrotic tissue, and the area is well drained.

Mortality after perineal prostatectomy is lower than after suprapubic. Wildbolz reports a mortality of 15 per cent in 105 suprapubic operations in contrast to a mortality of only 6.5 per cent in 305 perineal operations. In 29 of Wildbolz' cases, healing of the perineal fistula was delayed. In 1 case, the fistula persisted for more than three months. In 3 cases, there was a persistent urethrorectal fistula which required another operation for relief. Partial incontinence lasting for a few weeks was observed in 6 cases, and in 5 others it persisted for more than four months.

In discussing indications for prostatectomy, Hunt³⁴ says that inability to empty the bladder and persisting residual urine are the outstanding and important indications for prostatectomy. The absence of residual urine, however, does not constitute contraindication to operation if the gland is enlarged and there are subjective symptoms. With any amount of residual urine as a result of prostatic obstruction, the indications for operation are clear: with frequency, difficulty, pain and other symptoms, but with slight enlargement of the gland and no residual urine, the advisability of operation is questionable.

Death following prostatectomy has been due to the following causes, in order of frequency: (1) coexisting or preexisting cardiovascular, renal and pulmonary diseases; (2) surgical accidents, such as hemorrhage, and (3) postoperative complications. In recent years, effort has been directed toward providing factors of safety which tend to eliminate

34. Hunt, V. C.: Immediate and End Results of Suprapubic Prostatectomy. A Consideration of the Factors Involved, *Canad. M. A. J.* 17:1497, 1927

the orifice, and the tampon is removed by pulling gently on the thread emerging from the wound. In removing the tampon, the coils of Penrose tubing are gently manipulated, and these tend to unfold themselves, leading to little discomfort.

[ED. NOTE.—The use of coiled Penrose tubing as a tampon is perhaps a new feature. One can imagine that it would be difficult in all cases to get such a tampon to fit snugly enough for hemostasis at all points of the capsule. The pull of a thread through the urethra also would possibly be associated at times with cutting into the urethral tissue at the region of the bulb or triangular ligament and might call for a considerable amount of adjustment. The principle of counterweight traction is not without virtue, although the attachment of the weight to a Hagner-Pilcher bag would seem more likely to produce less discomfort, hemostasis would be better because of more uniform contact of the bag with the prostatic capsule, and the removal of the bag might be more certain and less difficult as a rule than that of coils of Penrose tubing. Any type of persistent pull on the remaining muscles at the neck of the bladder tends to increase the possibility of transient incontinence. The system of weights suggested by Ware would at least offer consistent tension and be free from the irregularly strong and weak tension occurring when the urethral tube of the hemostatic bags is attached to the patient.]

Thomas ³⁶ states that according to estimates, 50 per cent of patients with prostatic disease die within five years after the onset of obstruction, and that catheter life shortens this to two and a half years.

The function of the kidney is one of the most important factors in determining the qualifications of a patient for operation. An estimation of the urea nitrogen in the blood and the quantitative percentage output of phenolsulphonphthalein are the most commonly used tests of renal function. Normal values of urea nitrogen in the blood range from 12 to 20 mg. per hundred cubic centimeters; safe values range from 20 to 30 mg.; values of above 30 mg. should be regarded as dangerous, if not prohibitive of operation. The cardiovascular system and the blood are next to renal function in importance. As a result of the study on the cause of death following prostatectomy, Thomas notes the following rules: In cases in which low tension is present, when the systolic blood pressure is 110 or less, the diastolic must be more than 60; if the diastolic pressure is less than 60, the systolic must be more than 110. In cases in which high tension is present, when the systolic pressure is 180 or more, the diastolic must be less than 100; if the diastolic pressure is more than 100, the systolic must not be more than

36. Thomas, B. A.: *Vital Factors in the Management of Prostatic Obstruction*. Ann. Surg. 86:563, 1927.

The causes of the 42 deaths were as follows: uremia and renal insufficiency, 10; pulmonary embolism, 9; general sepsis, 7; cardiovascular disease, 6; secondary bleeding, 4; pneumonia, 3, and bleeding duodenal ulcer, general peritonitis, and erysipelas, 1 each. Renal insufficiency and uremia are important factors in cases in which urinary obstruction and retention have existed for a long time. Pulmonary embolism has not occurred as a cause of death since the adoption of preoperative preparation of all patients. It has continued to be difficult to combat general sepsis, which usually emanates from an acute exacerbation of cysto-ureteropyelonephritis. It would seem that prostatectomy had little to do with some of the deaths, but these deaths are included in the surgical mortality.

The late results were good. The preoperative difficulty in urination was relieved in 95 per cent of the patients.

Ware³⁵ condemns the packing of the prostatic capsule with gauze tampons, as ineffective and cumbersome. The Hagner and Pilcher bags overcome the disadvantages of gauze tampons, but these bags come in contact with the prostatic bed by drawing taut the rubber tube at its exit from the urethra and maintaining this pull by anchorage to a cradle with its points of support on the pelvis. These cradles are at times difficult to adjust and hamper the movements of the patient. Ware has devised a method which he believes is superior. On completion of enucleation, a Nélaton catheter is introduced until the vesical end becomes visible or can be palpated. A length of water-proofed linen fishing line is secured to the vesical end drawn into the wound. The catheter is withdrawn until a length of thread emerges which passes over a pulley at the foot of the bed and reaches the floor. Some Penrose tubing is secured to the thread emerging from the abdominovesical wound by throwing a knot about loosely coiled folds of the tubing arranged in roset fashion, or with greater refinement transfixing loops of tubing with the same thread armed with a large needle. When this is accomplished, the thread coursing through the urethra is pulled on, causing the rubber tampon to follow until the resistance of the prostatic bed at the introitus of the bladder is felt. Traction is sustained by applying a sand bag weighing from 3 to 5 pounds (1.4 to 2.3 Kg.) to the end of the thread, which is allowed to fall over the end of the operating table. When the patient is put to bed, the end of the thread, with its weight, plays over a pulley. The weight may be adjusted to the comfort of the patient. A thread attached to the tampon is allowed to emerge from the suprapubic wound at the time of closure.

In from forty-eight to seventy-two hours, when the need for hemostasis is past, the thread emerging from the urethra is cut close to

35. Ware, M. W.: Sustained Counterweight-Traction in Hemostasis of Prostatectomy, *Ann. Surg.* 86:561, 1927.

There is a marked and rapid increase in the volume of the gland. The diagnosis is frequently confused with that of carcinoma of the prostate. A single lump on the surface of the prostate usually means the onset of malignancy. Numerous irregularities and lumps suggest prostatitis. Pus in the expressed prostatic secretion and the presence of eosinophilia help confirm a diagnosis of infection.

It is easier to make a diagnosis in acute cases, and these are more significant on account of the urgency of treatment. Prostatectomy is the procedure to be used, preferably in two stages. In acute forms, however, when the condition of the patient does not permit delaying operation, perineotomy must be performed to permit evacuation of the pus. At the same time, the bladder should be drained.

Casariago³⁹ advises perineal prostatotomy as the treatment for patients with urinary retention due to acute gonorrheal prostatitis; the posterior surface of the prostate is exposed by means of a deep longitudinal incision over both lobes. Persistence of retention of urine in a case of acute gonorrheal prostatitis is a sign of formation of abscess with more or less destruction of the gland. Prostatotomy avoids this and prevents the formation of caverns and fistulas of the prostate. It may often be considered as prophylactic treatment of chronic prostatitis.

Calculi.—Thomas and Robert⁴⁰ give an extensive review of the literature on prostatic calculi and report three cases. Although cases have been reported occasionally in the older literature, it usually was not considered that the stones originated in the gland itself. In more recent times, however, prostatic calculi have ceased to be a rarity; they are, in fact, much commoner than the number of reported cases would indicate. The etiologic factor of true prostatic calculi is still hypothetical. These calculi, whether septic or aseptic, have as a nucleus the corpora amylacea, which are albuminoid or nitrogenous-like bodies. They are usually multiple and the size of a "millet seed" or a "pea"; they are most common in middle and late life and are associated with other pathologic conditions. About 65 per cent do not cause symptoms and are found accidentally during routine roentgen-ray examination or at operation. A persistent and rebellious prostatitis should arouse suspicion of calculi. Serious sequelae, such as abscess and gangrene, are rare. Malignancy and inflammatory nodules can be differentiated in almost 100 per cent of cases by means of roentgenograms. Phleboliths must be taken into consideration. Surgical intervention by the perineal route is the procedure of choice, except in cases in which the calculus communicates with the urethra, when it may be removed through the urethroscope.

39. Casariago, A. G.: Prostatotomy as Treatment of Urinary Retention Due to Acute Gonorrheal Prostatitis, *J. Urol.* 18:401, 1927.

40. Thomas, B. A., and Robert, J. T.: Prostatic Calculi, *J. Urol.* 18:470, 1927.

175. This is not so-called "pulse pressure" in its usual sense, but rather pulse pressure with systolic and diastolic limitations. Thomas has performed operations successfully in cases in which the systolic pressure was less than 110, or even 100, but the diastolic was always more than 60; conversely, he has had cases in which the diastolic pressure was less than 60, but the systolic was always more than 110. On the other hand, if the systolic pressure is more than 190, operation is a hazardous procedure, but it has been performed successfully several times when the diastolic pressure was less than 100; conversely, in many cases in which the diastolic pressure was as high as 120, prostatectomy has been performed with recovery, but the systolic pressure was invariably less than 175.

Age, in itself, is never a vital factor in prohibiting operation on the prostate. Thomas believes that it is unwise to force old men out of bed too soon. The many complications incident to epididymitis, to phlebitis and to embolism will thereby be averted.

Lowsley and Harrah³⁷ report a case of complete retention of urine in a man, aged 32, due to solid tumefaction of the prostate gland. Suprapubic cystostomy was performed.

The patient was subjected to suprapubic cystotomy under local anesthesia. Examination of the interior of the bladder revealed a rather firm mass about 4 cm. in diameter, extending from the floor of the neck of the bladder. A specimen was taken from this tumor-like projection and sent to the laboratory for examination. The bladder was drained by suprapubic suction for a period of fourteen days, after which the prostate was removed suprapubically under sacral and parasacral and regional anesthesia.

The growth had greatly increased in size since the first operation. Microscopic examination showed chronic inflammation suggestive of Hodgkin's lymphogranuloma.

Prostatitis.—Le Roy³⁸ reviews a series of thirty-four cases of suppuration in prostatic hypertrophy. He believes that these conditions are relatively common and often pass unnoticed, because at times the pain is only moderate, and pyuria, the patient's general condition, and the absence of unusual symptoms are not suggestive of the principal disease. Prostatic suppuration calls for energetic and immediate treatment; otherwise serious complications set in.

The urine is often clear, and, unless a rectal examination is made, the diagnosis may not be apparent until the condition is far advanced. The patient complains of a heavy feeling in the perineum and dysuria.

37. Lowsley, O. S., and Harrah, F. W.: Enlargement of the Prostate Gland with Characteristics Resembling Hodgkins' Disease, *Ann. Surg.* **86**:559, 1927.

38. Le Roy, C. M.: Des suppurations locales dans l'hypertrophie de la prostate. *J. d'urolog. méd. et chir.* **23**:311, 1927; **23**:388, 1927.

Schüppel⁴² states that cystitis gangraenosa desiccans is the most unfavorable form of inflammatory disease of the bladder. The name was given to this disease by Stöckel, who first described it and reported two cases. Although it is not possible to determine the number of reported cases, many have been observed.

The prognosis is grave. In Subotski's 167 cases, there were 90 deaths. Constantini reports 18 (40 per cent) deaths in a group of 45 women and 17 (51.5 per cent) in a group of 33 men. Houltani reports 8 (24.2 per cent) deaths among 33 pregnant women. This high mortality in women is explained by the association of this condition with unsuccessful abortion and adherent retroflexed uterus. The lower death rate among women in general is due to the fact that the urethra is shorter and permits more satisfactory drainage of the bladder. In men, prostatic disease, urethral stricture and tabes dorsalis are responsible for most of the deaths.

Successful treatment depends on an early diagnosis, which necessitates a study of the underlying causes. Frönstein classifies the cases into four groups:

1. The destructive factor began with some type of chemical which had been introduced into the bladder in too strong a concentration. In one case the condition was brought on by the introduction of 100 cc. of 20 per cent potassium permanganate, in another by the injection of 10 per cent sodium bromide for cystography.

2. In this group, the condition was caused by external pressure, such as retroflexion of the uterus, and urinary retention due to urethral stricture and prostatic hypertrophy.

3. The infectious cystitis had existed for a long time and gradually changed to a gangrenous type without mechanical factors.

4. In this group, the condition followed diphtheria, roentgen-ray therapy, impaction of calculus in the urethra, and extension from inflamed appendix.

The best treatment is the establishment of free drainage, following cystotomy. Any urinary obstructions should be relieved. Many cases go on to the stage of contracted bladder with consequent infected ureterohydronephrosis. Occasionally, the contraction of the bladder is so marked that help is obtained only by plastic operations. Schüppel cites a case in which there were multiple urethral strictures.

Decompression.—Bonneau⁴³ states that in the presence of marked distention of the bladder in patients who have not been catheterized and

42. Schüppel, A.: Ueber cystitis gangraenosa dissecans und die Therapie ihrer Folgen, Arch. klin. Chir. 145:380, 1927.

43. Bonneau, M. R.: Evacuation lente de la vessie par drainage sus-pubien filiforme avant la cystostomie, Presse méd. 2:1350, 1927.

BLADDER

Gangrene.—Carson⁴¹ reviews 167 cases of necrosis and gangrene of the urinary bladder noted in the literature and added 6 cases in which necropsy was performed at the University of Maryland. Necrosis or gangrene of the bladder occurs as a result of: (1) interference with the circulation, internal or external pressure; (2) infection, general or local, with or without mechanical injury; (3) lesions of the central nervous system, and (4) chemical irritants.

There were 116 females and 57 males. The age varied from 3 to 75 years, the majority of patients being in the third and fourth decades.

Of the 173 patients, 102 died, 67 recovered and 4 were not traced. In 40 cases, the gangrene occurred in pregnant women; in 23 it occurred after labor; in 15 it was associated with retention of urine; in 11 females it was due to external pressure with retention in 6. Cystitis was the antecedent in 14 cases (7 males and 7 females). The cystitis was complicated by retention in 7 of the 14 cases by stricture of the male urethra in 9 cases, in which there were calculi in the urethra in 3. In 6 cases prostatic obstruction with retention was present, in 6 calculi in the bladder with retention, and in 6 irritants were a factor and retention was associated. General infections played a part in 15 cases, in 7 of which there was retention. In 12 cases there were lesions of the central nervous system, retention being present in 7. Trauma was the cause in 5 cases; retention was associated in 3 of these. Extroversion of the bladder through the urethra occurred in 5 cases. There were 20 miscellaneous cases, retention being an added factor in 10 of these. In all, retention was present in 76 (48.5 per cent).

Obstruction of the circulation will explain the cases of simple necrosis, but pathogenic bacteria must be present before putrefaction can take place.

In the 67 cases in which the patients recovered, the diagnosis was made by cystoscopic examination, suprapubic cystotomy or examination of the exudate passed by urethra.

At necropsy, the mucosa of the bladder was frequently found to be yellowish, greenish yellow, or black with a putrefactive odor, and the perivesicular tissues showed evidences of varying degrees of inflammatory reaction, trigonitis, peritonitis and ureteritis.

[ED. NOTE.—In view of the clinical rarity of gangrene of the bladder, Carson's excellent review is timely. From a pathologic standpoint, regardless of the exciting factor, one must feel that ultimate interference with the vesical blood supply to such an extent as to destroy nutrition is the real cause of the condition. This presupposes a fulminating infection, intense irritation, or severe trauma, as is borne out by the cases reported.]

41. Carson, W. J.: Gangrene of the Bladder, *Ann. Surg.* 85:240, 1927

In this way, the necrosis and bleeding can be cleared up and the tumor reduced in size sufficiently to allow further treatment with electro-coagulation.

According to experiments on animals carried out by Drexler and Ginberg, chemocoagulation apparently does not have any permanent injurious effect on the normal mucosa of the bladder.

Ulceration.—Dean ⁴⁵ reports three cases of ulceration of the bladder, a late effect of applications of radium to the uterus. These cases are usually seen by urologists, and the symptoms and appearance suggest carcinoma of the bladder, but a tumor is not present.

There is often a history of irradiation with radium to a nearby organ, and there is an area of necrosis at the site nearest the application of radium. A histologic section is at times necessary to rule out a diagnosis of carcinoma or tuberculosis. There is an interval of at least a year between the time of the irradiation and the onset of symptoms.

The distressing subjective symptoms have been relieved readily by a prescription consisting of sodium citrate, 20 Gm., tincture of hyoscyamus, 25 cc., and enough cinnamon water to make 120 cc., given 1 teaspoonful in water two hours after each meal.

The most satisfactory treatment for the lesion consists of injections of mercurochrome-220 soluble into the empty bladder. To prevent undue irritation, the earlier instillations consist of 15 cc. of a 1:200 dilution, administered three times a week. Later, when healing results in greater toleration, the strength of the solution may be increased gradually to 2 per cent, the same quantity being used as before at the same time intervals. It is important that this treatment be carried on with regularity and persistence.

[ED. NOTE.—In some cases, it is almost impossible to distinguish between radium irritation, ulceration or malignancy of the bladder, especially in cases in which radium has been applied for primary tumor of the bladder. The area in the bladder is usually reddened, raised and edematous, and has all the appearances of a primary lesion of the bladder. Another point is that brought out by Dean in this paper that there are sometimes intervals of at least a year between irradiation and the onset of the symptoms.]

Exstrophy.—Colby ⁴⁶ reports a case of exstrophy of the bladder in a boy, aged 7. At one operation the left ureter was isolated from the bladder and transplanted to the sigmoid. Three weeks later at a second operation, the right ureter was transplanted to the cecum; it was neces-

45. Dean, A. L.: Ulceration of Urinary Bladder as Late Effect of Radium Applications to Uterus, *J. A. M. A.* 89:1121 (Oct. 1) 1927.

46. Colby, F. H.: Exstrophy of Bladder; Report of Case, *Boston M. & S. J.* 96:1033, 1927.

whose urine is normal, slow decompression of the bladder is of great advantage; he empties the bladder by means of a lumbar puncture needle of small caliber, introduced into the bladder suprapubically. The bladder is usually completely evacuated in twelve hours. The urinary equilibrium is reestablished, and secondary cystostomy may be carried out without risk to the patient.

Perrier, in discussing Bonneau's paper, states that he also makes a suprapubic capillary puncture in cases of marked distention. He reports a case in which this procedure was carried out on two occasions; the second was necessary on account of too long a delay before proceeding with the cystostomy.

Gerard, in cases of extreme distention, makes a small button-hole incision in the bladder through which he inserts a small catheter which is opened intermittently every other hour, permitting 200 cc. of urine to escape. The catheter is permitted to drain continuously after the fourth day.

[ED. NOTE—All stab or punch operations through the suprapubic region carry a moderate risk on account of possibility of injury to the peritoneum and urinary extravasation. The same results as those obtained by Bonneau can be carried out by various methods of decompression with a urethral catheter, notably that described by Foulds and Bumpus.]

Tumors.—Drexler and Ginberg⁴⁴ state that during the last eight years Joseph has treated more than fifty patients with benign and malignant tumors of the bladder either by chemocoagulation alone or by chemocoagulation combined with electrocoagulation. The technic is as follows: A cystoscope is passed and the bladder washed and filled as for cystoscopic procedure. A ureteral catheter with an open end is inserted through the cystoscope, and from 20 to 30 drops of freshly prepared solution of trichloroacetic acid is run over the upper surface of the tumor. The tumor becomes white due to action of the acid. After treatment the bladder is emptied and washed.

Patients with tumors situated in an area of the bladder inaccessible to the cystoscope can be treated with frequent instillations into the bladder of from 40 to 50 cc. of distilled water containing from 20 to 30 drops of trichloroacetic acid. Long-standing hematuria, the result of tumors of the bladder, can also be arrested in this manner. After two or three weeks either the tumor entirely disappears and is replaced by scar tissue, or it is reduced in size and is ready for further treatment.

Chemocoagulation is especially indicated in cases of carcinoma of the bladder with foul-smelling necrosis and bleeding with secondary cystitis.

44. Drexler, L. S., and Ginberg, W.: Treatment of Bladder Tumors by Chemocoagulation, *Surge. Gynec. & Obst.* 45:820, 1927.

[ED. NOTE.—Torsion of the cord is so frequently associated with descended or partly descended testes in which some developmental error is present that it is interesting to note the occurrence of the condition in the abdomen. Thus another infrequent type of lesion must be considered in the differential diagnosis of disease of the lower right quadrant. The absence of the testis from the scrotum might point to such a lesion if other features of the condition are not contradictory.]

Tumor.—Roeder ⁴⁸ describes a case of hyperplasia of the subperitoneal fat beneath the mesothelial coat (tunica vaginalis viscerum) of the testis. The patient had a left indirect inguinal hernia with a hydrocele of the tunica vaginalis. At operation, surrounding the cord and beneath the sac, was a continuous and complete layer of fat extending from the testis up to and through the internal inguinal ring. After the sac of hydrocele had been dissected away, a small nodule beneath the testicular layer of the tunica vaginalis was noted. This proved to be a lipoma, well encapsulated, and more intimately attached to the tunica vaginalis than to the tunica albuginea.

In reviewing the literature, attention is called to the fact that the scrotum embryologically is formed by a constriction of the walls of the lower part of the abdomen. The constriction includes the peritoneum and subperitoneal areolar tissue, the presence of which naturally favors the deposition of fat. Therefore, so-called fatty tumors of the testis should be regarded as hyperplasia of the subperitoneal fat originating from the areolar tissue beneath the tunica vaginalis viscerum or the testicular peritoneum. To be carefully differentiated, are masses of fat along the mesothelial tunics of the cord and fatty tumors in the region of the inguinal canal. Eight cases of lipoma of the testis are reported from the literature and analyzed. In the majority of these the tumor probably originated from the lower end of the cord and therefore cannot be classified as true testicular tumor, by the foregoing criteria.

[ED. NOTE.—In differentiating scrotal tumors one seldom thinks of the possibility of lipoma, a lesion which occurs surprisingly at times in other parts of the body. Roeder calls attention to the embryologic occurrence of this tissue in the scrotal contents and the clinical possibility of encountering such cases should be borne in mind.]

Infarction.—Lubash ⁴⁹ reports a case of infarction in the testis. The testis belongs to the same category as the kidney, spleen and brain, in that its circulation is terminal. Since infarction of the testis exists, it should be thought of as an entity.

48. Roeder, C. A.: Lipoma of the Testicle, *Ann. Surg.* 85:275, 1927.

49. Lubash, Samuel: Infarction of the Testicle, *J. Urol.* 18:421, 1927.

sary to use the cecum to receive this ureter to avoid tension. Photomicrographs of the tissue removed from the bladder showed numerous mucus-secreting glands.

[ED. NOTE.—The mucus-secreting surface, described by Colby, is common in most cases of exstrophy of the bladder; it is the result either of metaplasia of the normal covering or of hyperplasia of glands in the mucosa. Such glandular structure often shows characteristics of malignancy.]

TESTIS

Torsion.—Ormond⁴⁷ states that about 150 cases of torsion of the spermatic cord are on record, the first case having been reported by Delasiuave in 1840. It occurs most often near the age of puberty, although a few cases are reported shortly after birth and a few at 60 years or more. The condition has also been observed at birth. The right side is slightly more affected than the left. Developmental errors most often associated with undescended testes (52 to 69 per cent of cases) have been held to be a predisposing cause.

Etiologic factors mentioned are an abnormally loose scrotum, a voluminous tunica vaginalis, an unusually long gubernaculum, and an abnormal attachment of the cord to the testis. From a consideration of the anatomy, Ormond holds that the last two are the most probable etiologic factors. Ordinarily, the reflection of the parietal layer of the tunica over the epididymis forms a mesentery running from the globus minor up to the middle of the globus major. In most of the recorded cases of torsion, this has been much shortened and includes only the globus major, and the twist occurs in this very much shortened mesentery.

Ormond notes in the literature five cases of torsion in intra-abdominal testis and adds a case of his own, that of a man, aged 42, who had experienced intermittent right-sided abdominal pain for two days before admission. At operation a mass was found consisting of a black swollen testis, with one complete twist of its mesentery, the testis being adherent to the tip of the appendix. There was no evidence of malignancy, which had been noted in three cases in the literature. In only one case (Stiles) was preoperative diagnosis definitely determined.

In all these cases, the testis was on the right side. This is not true of torsion generally, although the right side is more frequently affected than the left, just as it is in maldescent of the testis, which seems to be the chief etiologic factor in torsion.

Ormond hypothesizes that torsion in the intra-abdominal testis may be found usually on the right side because of the presence of the cecum with its intermittent loading and pull on the peritoneum.

47. Ormond, J. K.: Torsion of an Intra-Abdominal Testis, *Ann. Surg.* 85:280, 1927.

Stricture of the ureter was seen in ten patients, three boys and seven girls. Diverticula and tumors of the bladder were also encountered.

It is shown that the urinary diseases of childhood resemble those of adult life, and that with practice, cystoscopy in children can be accomplished without difficulty, and may be useful for therapeutic procedure as well as for diagnosis.

Hunter and Montgomery⁵² follow up the work of Andrewes, who, when investigating the hypobilirubinemia indicated by the van den Bergh test in uremic serum, discovered a new type of diazo-reaction. On allowing the mixture of alcoholic extract from a uremic serum to stand in contact with the van den Bergh reagent for a period of twenty-four hours, Andrewes found that a pinkish-brown or buff color developed, and that when this was made alkaline with a strong alkali, a bright red color appeared immediately; this was stable for from a few minutes to more than half an hour according to its original intensity.

Hunter and Montgomery observed nephrectomized rabbits and dogs, and thus confirmed the work of Andrewes. As a result of their investigations, they modified the technic previously used and presented the following:

One gram of sulphanilic acid is added to a liter flask containing about 500 cc. of water and 15 cc. of 37 per cent (concentrated) hydrochloric acid. The contents are shaken at ordinary temperature till the sulphanilic acid has gone into solution. Water is then added and the contents mixed. The solution keeps indefinitely.

It is more convenient and reliable to have a stock 5 per cent solution of sodium nitrite than to make 0.5 per cent solutions at weekly intervals. Five grams of good quality sodium nitrite is dissolved in 100 cc. of water. This, if kept in a stoppered bottle in an icebox, is reliable for at least a year, and for several months without the latter precaution. One cubic centimeter of this solution is mixed with 9 cc. of water before each diazotization.

The test is performed by precipitating and centrifugalizing the serum or plasma with 2 volumes of 95 per cent alcohol, taking 1 cc. of the supernatant fluid in a small test tube, adding 0.4 cc. of the diazo-reagent and 0.1 cc. of concentrated hydrochloric acid. The tube is heated over a flame or in a water bath at about 80 C., for a minimum of two minutes. If the test is positive, the buff color will then have developed fully. The tube is cooled and 1 cc. of 2.5 normal solution of sodium hydroxide is added and the tube quickly inverted. The intensity of the red color thus produced accords with the buff color obtained in the acid solution. As the buff color is stable, it is the more suited for

52. Hunter, George, and Montgomery, R. C.: On the Diazo Reaction in Uremic Serum and in Normal Urine, *Canad. M. A. J.* 17:148, 1927.

The etiology, although still obscure, may be classified as follows: (1) predisposing, any condition that could cause embolism; (2) exciting, a temporary twist of the cord that may result in stasis in one of the arterioles. Infarction of testicle should be suspected in patients with temporary torsion whose symptoms return after abatement. The treatment is purely surgical in the form of orchidectomy.

URETHRA

Chauvin⁵⁰ distinguishes four groups of double urethra: 1. The complete double urethras which are more or less permeable canals extending from the bladder to a definite meatus; there is no connection between the two urethras. 2. The one-eyed juxtra-urethral ducts, which end in a culdesac at one or the other of the extremities open either into the bladder or to the exterior. 3. The bifurcation type of unique, and it is the anterior segment which bifurcates into two portions. At times the deep urethra is unique, and it is the anterior segment which bifurcates into two portions. In other cases the reverse disposition, in which the anterior is single and the posterior portion is double, is found. The accessory canal in this form may be on top, underneath or on the side of the principal urethra. 4. The fourth type comprises the canaliculized diverticula; they communicate by one of their extremities. In this type are merely small cellules which usually dip down into the spongy or prostatic urethra.

UROLOGIC DIAGNOSIS

Kretschmer⁵¹ points out that all adult patients who present symptoms of lesions in the genito-urinary tract are generally subjected to a complete urologic examination. This is not ordinarily the case with children, although infants and children are subject to almost all the urologic diseases of adult life, except enlargement of the prostate and carcinoma. As a matter of fact, small children can be subjected to a complete urologic examination. There are seven patients in this series under 12 months of age. The youngest was a boy, aged 27 days. Thirty-four of the patients were males and fifty-two were females.

The symptoms in children and adults are about the same in order of incidence: fever, pain, cloudy urine, frequency and hematuria.

In disorders of the kidney, pyelitis leads the list, followed by tuberculosis. The patients with persistent pyelitis were treated by pelvic lavage with solutions of silver nitrate.

50. Chauvin, E.: À propos des urètres doubles; en particulier de leurs variétés postérieures, *J. d'urolog. méd. et chir.* 23:289, 1927.

51. Kretschmer, H. L.: Urologic Problems in Infancy and Childhood, *J. Urol.* 18:433, 1927.

All cases of spontaneous cystitis, all cystitis resisting the usual treatment for this condition and recurring cases of cystitis suggest tuberculosis. In all cases of cystitis, except those following urethritis, cystoscopy should be carried out. Catheterization of the urethra should not be preceded by a general examination of the bladder. Any type of hematuria demands immediate urologic examination.

All patients with renal pyuria which is not definitely tuberculous require roentgen-ray examination. All roentgen-ray examination for renal stone should include the entire urinary tract.

The use of vaccines is often a "cache-misère," masking the physician's ignorance and his incapability of establishing a diagnosis of infection. The diagnosis should be made primarily, and vaccine should never be used unless other methods are useless.

Marion,⁵⁵ in discussing the value of phenolsulphonphthalein, insists on the following points: 1. One should always use phenolsulphonphthalein of the same origin. 2. In an intravenous injection, it is necessary that the entire amount be injected into the vein. 3. The measure of standard must be frequently renewed. 4. If the result is doubtful, the test must be repeated several times.

A patient eliminating large quantities of phenolsulphonphthalein can usually be considered as having good resistance. In cases in which the amount of phenolsulphonphthalein is found low on several occasions, the surgical outlook is usually poor.

The phenolsulphonphthalein test is more reliable than the so-called Ambard's "constant"; if fever is present, the constant improves, whereas the amount of phenolsulphonphthalein eliminated diminishes, giving a more accurate index of the condition.

Pescatori⁵⁶ cites a case which he called "false appendicitis." The patient had pain in the right hypochondrium, radiating into the ileocecal fossa and occasionally to the left side. A diagnosis of chronic appendicitis was made, but roentgenologic examination revealed a "bean-sized" stone in the left kidney. Roentgenograms of the gastro-intestinal tract were negative. Removal of the stone was followed by uneventful recovery. Pescatori calls attention to this case, and it is cited here to show the valuable use of the roentgen ray in differential diagnosis, a point in technic used in American urologic circles for a long time.

[ED. NOTE.—This report is of interest in that the clinical course is the opposite to that usually observed. Frequently, patients with urinary calculi are subjected to one or more abdominal operations before the true nature of their condition is determined. In a series of more than

55. Marion, G.: À propos de l'épreuve de la phénosulfophthaléine, *J. d'urolog. méd. et chir.* 24:57, 1927.

56. Pescatori, Guido: Sindrome appendiciteica da calcolosi renale sinistra rivelatasi ai raggi X, *abstr. Ztschr. f. urol. Chir.* 21:13, 1926-1927,

comparative tests. At any rate, it can be preserved until it is convenient to add alkali to a series of tubes at one time.

As originally pointed out by Andrewes, the secondary red color is produced only by the addition of strong alkali. This color will not develop with strong alkali in the presence of a large amount of ammonia, so that ammonium sulphate cannot be used in this test in association with alcohol to precipitate the proteins from the serum, as recommended by Thannhauser and Andersen for the van den Bergh test.

Their technic makes the test more sensitive and renders it less subject to interference. The substance giving the diazo-test in uremic serum is shown to be a normal, but as yet unidentified, urinary constituent.

Gottlieb and Strokoff⁵³ report several cases in which pneumopyelography was employed. They drew the following conclusions from their study: 1. This is a method of choice on account of the absence of irritation even in cases of hydronephrosis. 2. It permits the obtaining of pictures of stones which are not usually opaque in roentgenograms. 3. Only one roentgenogram, instead of two, is necessary to make the diagnosis. 4. Its technical application is simple and harmless when properly used.

[ED. NOTE.—Pneumopyelography has not been used extensively in this country. Apparently from reports in American periodicals the results are not so successful as reports from foreign clinics seem to indicate. As cystoscopy and pyelography are such satisfactory diagnostic procedures, and in most cases permit a precise diagnosis, pneumopyelography would have to be markedly improved before it is used to any extent in American clinics.]

Marion⁵⁴ gives a number of general principles in diagnosis and treatment of urologic conditions. He states that it is necessary to establish the diagnosis of a disease by relying on one physical symptom, such as pyuria or hematuria, rather than on a functional trouble, such as pain or frequent urination.

If, during urethral catheterization, obstruction is encountered in the region of the bulb of the urethra, a Béniqué catheter should be used and not a sound or a bougie of smaller caliber.

Hematuria in a patient with prostatic hypertrophy must not be attributed to the prostatic enlargement unless all other causes of hematuria have been eliminated.

A patient suffering from chronic urinary distention caused by prostatic hypertrophy should not be catheterized; the bladder should be drained and explored.

53. Gottlieb, J. G., and Strokoff, F. J.: *La pneumopyélographie*, J. d'urol. méd. et chir. 23:328, 1927.

54. Marion, G.: *Quelques grands principes directeurs du diagnostic et de la thérapeutique urologiques*, J. d'urol. méd. et chir. 23:194, 1927.

A choice is given of nitrous oxide, ethylene, spinal anesthesia, sacral block and local infiltration. Spinal anesthesia is disapproved because of its effect on the blood pressure, preference being given to sacral block and local infiltration, for suprapubic and scrotal operations and to regional block, local infiltration and analgesia by nitrous oxide oxygen for operations on the kidneys, at times to be supplemented with local infiltration.

In operations on the bladder and prostate, sacral block, combined with infiltration of the abdominal wall, is recommended, the technic of Hunt being followed. The wall of the bladder is also infiltrated, as well as the capsule of the prostate, if this is the point of attack. Usually this procedure will suffice, but the anesthetist must reassure the patient; if there is apprehension, he should be ready to administer nitrous oxide to the point of analgesia. The patient is for this reason given a preliminary hypodermic injection of morphine and atropine.

In the genito-urinary examining room, Lower prefers the use of procaine to cocaine as a urethral anesthetic, especially in operations such as urethrotomy. For cystoscopy 10 cc. of a 2 to 4 per cent solution of procaine is used. If a pyelogram is to be made, morphine is not given, as Lower believes that the patient should be sensitive to the pain of renal distention. In cases of tuberculosis of the bladder, sacral anesthesia finds a field of usefulness. It is contraindicated in punch operations because of the fact that complete relaxation of the neck of the bladder frequently follows sacral block. Local infiltration of the neck of the bladder, together with analgesia by nitrous oxide, finds a field of usefulness here.

In the case of old men with enlarged prostates, the combination of sacral block and abdominal wall infiltration is emphasized as being a life-saving procedure.

[ED. NOTE.—Lower expresses the thought of the more progressive urologists of the day. Sacral block is easily administered in the average case, and with infiltration of the abdominal wall as a rule no further injection of the bladder or prostate itself will be needed. If the anesthesia is properly administered, it may be said also that pain will as a rule be absent, and there will seldom be need for nitrous oxide or any form of anesthesia by inhalation unless it is given because of apprehension or mental confusion of the patient. Lower uses procaine as an anesthetic for the urethral mucosa. It has been the experience of most urologists that procaine has little surface action; in order to have an anesthesia with a satisfactory surface action, it is usually necessary to use cocaine.]

1,400 patients with renal stone, 50 per cent had had at least one operation and 20 per cent, two or more operations before the renal stone was removed. In a second series of 400 cases of ureteral calculi, either the gallbladder or the appendix had been removed in 23 per cent. In at least half of these cases, stones had been present in the left ureter.]

Jeck and Munch⁵⁷ point out the truth of the words of Watson, who says: "In the examination of urine for tubercle bacilli, the method which requires the fewer laboratory reagents, consumes less time, and gives a higher percentage of positive results is the one which will be used eventually." They, therefore, carried out a most thorough and convincing group of experiments, proving the value of simple centrifugalization as a method of identifying the bacilli of tuberculosis in the urine. They found that in examining any specimen of urine for the bacilli by centrifugalizing methods, the best results were obtained when the specimen was centrifugalized for a period of not less than fifteen minutes at a speed of approximately 2,300 revolutions a minute. Longer than fifteen minutes is apparently unnecessary.

Pus is important, as a centrifugalizing force, in carrying down the bacilli. According to certain established methods, part of the pus should be removed in order to produce better smears; then the pus removed should be examined for bacilli as well as the final sediment. Coincident centrifugalization of part of the unknown specimen to which bacilli from a stock suspension have been added and subsequent coincident staining of both smears on the same slide are advisable.

Simple centrifugalization as a means of finding the bacilli of tuberculosis in the urine is equal to any established method and better than most of them. It would, therefore, seem to be the most satisfactory method for the urologist who does his own laboratory work or who has it done under his own supervision.

Lower⁵⁸ favors the use of the anoci-association method of anesthesia from the standpoint of minimizing traumatic and psychic shock. The lipoid solvent anesthetics, such as ether and chloroform, have a special deleterious effect on the kidneys. Albuminuria follows their usage in about a fourth of the cases. In patients with diseased kidneys, the effect of inhalation anesthesia of this type may be enough to produce fatal urinary suppression or persistent albuminuria. Lower thus believes that the use of ether and chloroform is contraindicated in renal operations or when the urinary tract is already carrying an extra load.

57. Jeck, H. S., and Munch, Margaret A.: Studies in Centrifugalization as a Means of Identifying Tubercle Bacilli in the Urine, *J. Urol.* 18:607, 1927.

58. Lower, W. E.: Anesthesia in Genito-Urinary Operations, *Ann. Surg.* 86: 268, 1927.

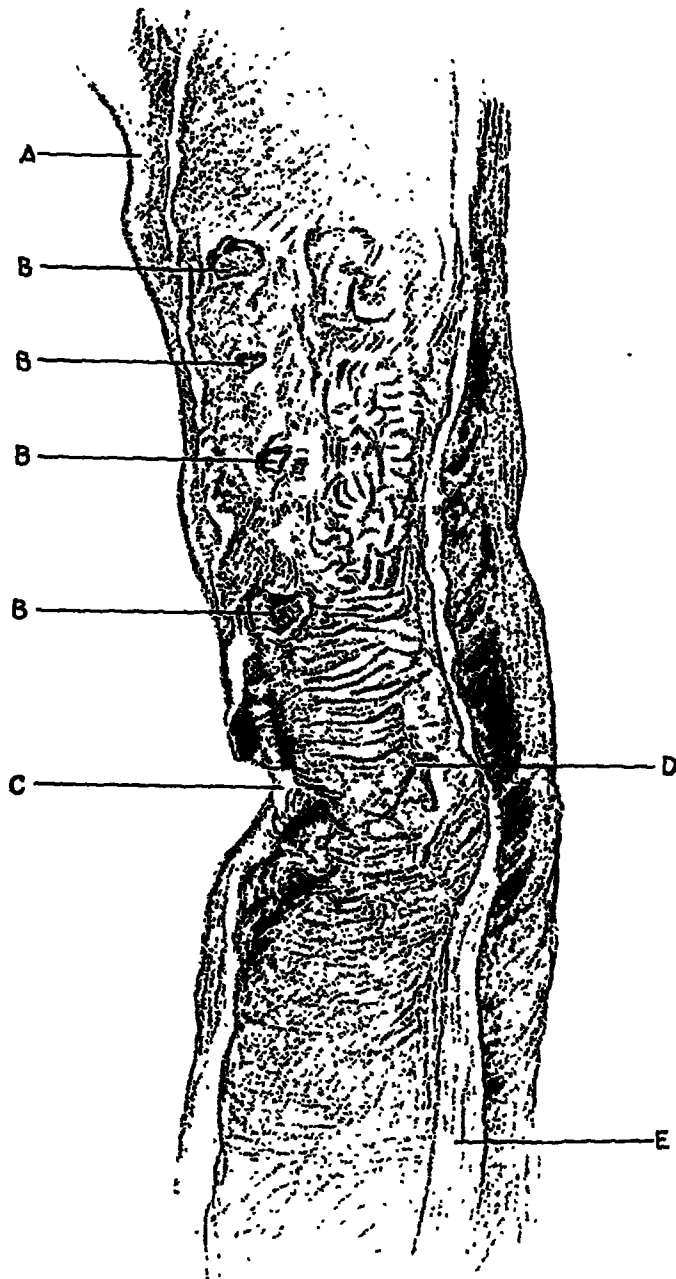


Fig. 1.—Postmortem specimen. *A* indicates the jejunum, adherent to surface of bowel; *B*, four smaller ulcers; *C*, the perforated ulcer; *D*, the narrowing and constriction of lumen, and *E*, marked hypertrophy of wall of colon proximal to ulceration and narrowing of lumen.

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SIMPLE, NONSPECIFIC ULCER OF THE COLON *

MAURICE E. BARRON, M.D.

BOSTON

Simple, nonspecific ulcer is a pathologic lesion which occurs in the colon. It may exist as a single lesion or it may be multiple. The fact that it does occur and usually tends to perforate should make one ever mindful of its occurrence.

By simple ulcer is meant an ulcerating lesion which is not due to the action of any specific organism such as the specific ulcer of tuberculosis, syphilis, ulcerative colitis, dysentery, typhoid fever or to the local action of any chemical agent, and which is not secondary or above a malignant tumor causing constriction.

This series comprises fifty-three cases; fifty were collected from the literature and three are cases that I observed. In this series, the cases include simple ulcers of the colon regardless of their location. Both perforated ulcers and chronic latent ulcers have been considered, since in certain patients the ulcers may have been multiple, one ulcer having perforated and the others remaining quiescent. I have included also simple ulcer of the rectum as I believe the etiology and pathology of this disease to be the same as that of simple ulcer on any segment of the colon. I have also included those simple ulcers which, in the process of healing, have caused a stenosing cicatrix, and thus given rise to partial or complete obstruction. In other words, all ulcers of the colon of a nonspecific nature that were studied by autopsy, resection or visualization at time of operation were included.

HISTORICAL

There is nothing in the American literature regarding this lesion aside from a case report by Lyle,¹ in 1912, and a report of three cases by Dickinson,² in 1922, entitled, "Perforating Ulcers of the Cecum." Most of the cases reported are found in the French and German literature.

This disease is not new, and was first described by Cruveilhier³ in 1830. Since then, there have been many cases reported. No attempt

* From Surgical Department of Beth Israel Hospital, Boston, Mass.

1. Lyle, H. H. M.: Simple Ulcer of the Colon: Perforation, *Ann. Surg.* 56:473, 1912.

2. Dickinson, G. K.: Perforating Ulcers of the Cecum, *J. A. M. A.* 78:1792 (June 10) 1922.

3. Cruveilhier, J.: Rectum, *Atlas d'anatomie et pathologie*, 1830-1832, p. 4.

TABLE 1.—*Résumé of Cases Reported Since 1837*

| Author | Sex | Age | Preoperative Diagnosis | Location | Perforation | Result |
|--|---------------|--------------|---------------------------------------|---------------------------|----------------|---|
| 1. Marchesseaux: Bull. Soc. anat. de Paris 12:343, 1837 | F | 45 | Intestinal perforation or peritonitis | Rectum | Perforation | Autopsy |
| 2. Rogee: Bull. Soc. anat. de Paris 13:181, 1838 | F | 61 | No diagnosis | Rectum | Perforation | Autopsy |
| 3. Greenhow: Path. Soc. Newcastle & Caley, Dec., 1848 | M | 72 | No diagnosis | Splenic flexure | Perforation | Autopsy |
| 4. Lebert: Traité d'anatomie et pathologie, générale et spéciale, 1861, vol. 2, p. 206 | M | 47 | No diagnosis | Splenic flexure | Perforation | Autopsy |
| 5. Idem | M | 47 | Intestinal obstruction | Sigmoid | No perforation | Autopsy |
| 6. Dujardine: Soc. de sc. méd. et Naturelle de Bruxelles, 1864 | M | No age | Tumor of spleen, colitis | Splenic flexure | Perforation | Autopsy |
| 7. Claus: Inaug. Diss., Zurich, 1856 | M | 47 | Peritonitis | Splenic flexure | Perforation | Autopsy |
| 8. Dickinson: Tr. Path. Soc. London 18:101, 1867 | F | 42 | Peritonitis | Sigmoid | Perforation | Autopsy |
| 9. Idem | M | 42 | Renal disease | Descending colon | Perforation | Autopsy |
| 10. Robin: Thèse, Paris, 1869 | M | 66 | No diagnosis | Descending colon | No perforation | Autopsy |
| 11. Costin: Brit. M. J. 2:247, 1870 | M | 45 | No diagnosis | Ascending colon | Perforation | Autopsy |
| 12. Lepine: Bull. Soc. anat. de Paris 45:27, 1870 | F | 70 | No diagnosis | Splenic flexure | No perforation | Autopsy |
| 13. Chouppe: Bull. Soc. anat. de Paris 45:322, 1870 | M | 32 | No diagnosis | Hepatic flexure | Perforation | Autopsy |
| 14. Demange: Rev. méd. de l'est, Aug., 1897, p. 500 | M | 72 | No diagnosis | Sigmoid | Perforation | Autopsy |
| 15. Mickle: Brit. M. J. 1:637, 1883 | M | 45 | Peritonitis and perforation | Sigmoid | Perforation | Autopsy |
| 16. Bradbury: Lancet 2:637, 1884 | M | 30 | No diagnosis | Cecum | No perforation | Autopsy |
| 17. Oliver: Lancet 1:424, 1885 | No age or sex | No diagnosis | No diagnosis | Ascending colon | Perforation | Autopsy |
| 18. Parker: St. Barth. Hosp. Rep. 23:213, 1887 | F | 18 | Perityphilitis | Ascending colon | Perforation | Autopsy |
| 19. Idem | F | 49 | No diagnosis | Ascending colon and cecum | Perforation | Autopsy |
| 20. Ollier: Loire méd. 11:3, 1892 | M | 56 | Peritonitis | Cecum | Perforation | Autopsy |
| 21. Morel and Scheyron: Soc. de méd. de Toulouse, 1895 | M | 46 | Cancer of cecum | Cecum | No perforation | Examination resected tissue, cured |
| 22. Southam: Brit. M. J. 1:254, 1895 | M | 67 | No diagnosis | Cecum | Perforation | Autopsy |
| 23. Guinard: Thésis, Paris, 1896, no. 324 | M | 27 | No diagnosis | Hepatic flexure | Perforation | Autopsy |
| 24. Morel and Rispail: Soc. de méd. de Toulouse, 1896 | M | 67 | Intestinal obstruction | Sigmoid | Perforation | Autopsy |
| 25. Gamgee: Brit. M. J. 1:950, 1898 | M | 28 | No diagnosis | Sigmoid | Perforation | No autopsy or pathologic examination, cured |
| 26. Quenu and Duval: Rev. de chir. 26:692, 792, 1902 | F | 50 | Ulcer of rectum | Rectum | No perforation | No autopsy, cured |
| 27. Tedenat, quoted by Quenu and Duval | M | 40 | Paracecal abscess | Ascending colon | Perforation | No autopsy, cured |
| 28. Idem | M | 52 | No diagnosis | Cecum | Perforation | Incomplete autopsy |
| 29. Idem | M | 68 | No diagnosis | Ascending colon | Perforation | No autopsy, cured |
| 30. Ziekler: Beitr. z. klin. Chir. 67:189, 1910 | F | 25 | Appendicitis | Ascending colon | Perforation | No autopsy, cured |

was made to collect a group of these cases for study until 1902. At that time, Quenu and Duval⁴ reviewed twenty-seven cases of simple ulcer of the colon reported in the literature, including their own case which presented an ulcer of the rectum. Twenty-five of these patients were studied both in life and at postmortem examinations. Autopsy was incomplete in one case and in another case a histologic and gross study of the resected lesion was made.

In 1920, R. Soupault⁵ reviewed twenty-seven cases of perforated ulcers of the colon. In his series, he eliminated ulcers of the rectum, ulcers situated above a stricture, ulcers causing stricture, though the strictures be due to a healed ulcer, and latent ulcers that have not perforated. Since then there have been several cases reported both in the French and German literature.

A brief historical résumé of the cases reported since 1837 is given in the following table.

REPORT OF AUTHOR'S CASES

CASE 1.—History.—Mr. S. B., a carpenter, aged 55, entered the surgical service of the Beth Israel Hospital on Nov. 4, 1926, with a complaint of pain in right lower quadrant. His family and past history were essentially negative. About two months previously, he had had an attack of pain in right lower quadrant which was not sharp or radiating. At that time, it was not severe enough to keep him in bed. The pain lasted one and a half days and was not associated with nausea or vomiting. The day before entrance to the hospital, he had a similar attack, but much more severe. Pain was localized just to the right of McBurney's point, causing him to double up. He was unable to work at this time. At no time previous to this history had he complained or consulted a physician for any abdominal condition. He was markedly constipated, always using cathartics. There never had been any nausea or vomiting. His stools varied in shape, and he described the color as being like that of weak tea. For two years he had had epigastric distress after meals. He weighed 171 pounds (77.6 Kg.). He had never been jaundiced.

Physical Examination.—The patient was a well developed and well nourished, middle-aged man, lying in bed with no objective signs of pain. The skin was moist and the face flushed. There was nothing else of note except marked tenderness of the whole right side of the abdomen. The maximum tenderness seemed to be in a line slightly above McBurney's point on the level with the umbilicus. There was a slight spasm in this region. The costovertebral angles were not tender. The abdomen was tympanitic throughout. No definite mass was made out over the tender area. A provisional diagnosis of acute appendicitis was made, and immediate operation was advised. The results of the urinalysis were negative. Examination showed: white blood cells, 12,300; temperature, 100 F.; the pulse rate, 100, and respiration, 22.

Operation.—Nov. 4, 1926: A right rectus incision was made under ether anesthesia, and a small amount of free fluid escaped from the peritoneal cavity. A

4. Quenu, E., and Duval, P.: Simple Ulcer of the Large Intestine, *Rev. de chir.* 26:692, 792, 1902.

5. Soupault, R.: Contribution to the Study of the Perforation of Simple Ulcer of the Colon, *Rev. de chir.* 58:480, 1920.

The following report was made at this time from the x-ray department: The tone of the stomach was good, and peristalsis was normal; the outline of the stomach was regular while the duodenum showed constant irregularity. Examination made five hours after the ingestion of the barium meal showed a small residue in the stomach (from 10 to 15 per cent). The head of the meal was in the distal portion of the colon (hypermotility). Examination made twenty-four hours after the barium meal showed the head of the meal in the ampulla of the rectum. The entire colon was empty. Examination of the colon with an opaque enema did not show any obstructive lesions. The cecum and ascending portion of colon showed finger-like defects, but its outline was rather smooth. The terminal ileum was well filled, distended, and also showed irregular filling. The inferior border of the transverse portion of colon was slightly irregular and appeared to be fixed.

The hypermotility of the colon when examined five hours after the barium meal and also the rapid emptying of the colon after the twenty-four hour examination suggested marked colonic irritation. This, together with the filling defect in the terminal ileum, cecum and ascending portion of the colon, definitely pointed to a pathologic process in that region. The entire picture was not characteristic of a malignant condition. There was a possibility of a tuberculous lesion.

The patient did not appear again until his next admission to the hospital on Aug. 15, 1927. This was the first time that he came to my attention. Again, the chief complaint was pain in right side of the abdomen. The patient said that he had been operated on at the Beth Israel Hospital seven months before. He had been discharged as cured, but he had never felt well since his operation. The week before his second admission, the pain was rather severe and stabbing, and seemed to be getting worse. The family physician said that he had felt a tumor in the patient's right side since he left the hospital, and that the tumor was now growing larger. His appetite was good. During the past four days, he had been constipated, requiring enemas. Previous to this, he said that he had had bowel movements about eight times a day; the stools were watery and accompanied by considerable gas. There had not been any nausea or vomiting. His best weight was 210 pounds (95.2 Kg.) one year before admission to the hospital. At the time of the previous operation, he weighed 171 pounds (77.6 Kg.); his present weight was 164 pounds (74.4 Kg.).

On his discharge from the hospital after his previous operation, he gained in weight, but recently he had been losing. His past history and family history were the same as on the previous admission. The physical examination was essentially the same, except for the abdominal examination. There was a scar over the right rectus muscle as a result of the previous operation. His right side was rigid and spastic all over. There was a palpable mass about the size of a small grapefruit which seemed to be somewhere in the center, between the right iliac fossa and the right costal margin. This mass was extremely tender to the touch. The left side of the abdomen was soft and tympanitic throughout and tenderness was not noted. A provisional diagnosis of malignancy of the colon with a secondary inflammation was made. The patient had a slight elevation of temperature; the pulse rate was not increased. An x-ray report two days after admission showed the following: The tone of the stomach was good; peristalsis was normal; the outline was regular, and the duodenum did not show any filling defect but appeared to be fixed. Examination five hours after the ingestion of a barium meal in the stomach showed the head of the meal in the sigmoid flexure. The entire colon was well filled. The cecum was irregular and showed a definite filling defect. Examination twenty-four hours after the barium meal showed

TABLE 1.—Résumé of Cases Reported Since 1837—Continued

| Author | Sex | Age | Preoperative Diagnosis | Location | Perforation | Result |
|--|---------------|--------|--|-----------------|----------------|--|
| 31. Lyle: Ann. Surg. 50: 473, 1912 | F | 20 | Appendicitis | Ascending colon | Perforation | No autopsy, cured |
| 32. Kunkle: Deutsche Ztschr. f. Chir. 147: 234, 1918 | M | 53 | Strangulated hernia | Hepatic flexure | Perforation | Autopsy, |
| 33. Soupault: Rev. de chir. 58: 480, 1920 | F | 22 | Appendicitis | Ascending colon | Perforation | No autopsy, cured |
| 34. Bazy: Bull. et mém. Soc. de chir. de Paris 46: 416, 1920 | M | 65 | Obstruction, cancer | Ascending colon | Perforation | Autopsy |
| 35. Idem | M | 20 | Appendicitis | Cecum | Perforation | No autopsy, cured |
| 36. Gregoire: Bull. et mém. Soc. de chir. de Paris 46: 420, 1920 | M | 55 | Appendicitis | Sigmoid | Perforation | No autopsy, death |
| 37. Sleur: Bull. et mém. Soc. de chir. de Paris 46: 421, 1920 | M | 30 | No diagnosis | Cecum | Perforation | Autopsy |
| 38. Lardennols: Bull. et mém. Soc. de chir. de Paris 46: 447, 1920 | M | 52 | Peritonitis | Cecum | Perforation | Autopsy |
| 39. Schoemaker, quoted by Soupault | M | No age | Peritonitis | Sigmoid | Perforation | Autopsy |
| 40. Levy: Deutsche Ztschr. f. Chir. 165: 366, 1921 | M | No age | Appendicitis | Cecum | No perforation | No autopsy, cured |
| 41. Ecot and Richard: Bull. et mém. Soc. anat. de Paris 92: 138, 1922 | No age or sex | | Obstruction | Ascending colon | Perforation | No autopsy, cured |
| 42. Dickinson: J. A. M. A. 78: 1792 (June 10) 1922 | M | No age | Appendicitis | Cecum | Perforation | Autopsy |
| 43. Idem | M | 22 | Chronic appendicitis, chronic cholecystitis | Cecum | Perforation | Autopsy |
| 44. Idem | M | 56 | Appendicitis | Cecum | Perforation | No autopsy, cured |
| 45. Bowen: Guy's Hosp. Rep. 72: 441, 1922 | F | No age | Intestinal perforation | Sigmoid | Perforation | No autopsy, death |
| 46. Idem | F | 27 | No diagnosis | Cecum | Perforation | No autopsy, does not state |
| 47. Challer and Mallet-Guy: Arch. d. mal de l'app. digestif. 13: 521, 1923 | M | 50 | Tuberculous peritonitis, tuberculous enteritis | Ascending colon | No perforation | Autopsy |
| 48. Mintz: Zentralbl. f. Chir. 50: 1208, 1923 | F | 18 | Intussusception | Cecum | No perforation | Resection, pathologic examination, cured |
| 49. Broere: Nedrl. Tijdschr. v. Geneesk. 67: 2274, 1923 | F | 80 | No diagnosis | Sigmoid | Perforation | Autopsy |
| 50. Boss: Beitr. z. klin. chir. 140: 40, 1927 | M | 38 | No diagnosis | Sigmoid | Perforation | No autopsy, cured |
| 51. Barron: In the text..... | M | 56 | Appendicitis, malignancy | Ascending colon | Perforation | Autopsy |
| 52. Barron: In the text..... | F | 23 | Appendicitis | Cecum | No perforation | No autopsy, cured |
| 53. Barron: In the text..... | F | 32 | Simple ulcer of rectum | Rectum | No perforation | No autopsy, cured |

large, inflammatory mass was found at the hepatic flexure, firmly tied down to all the adjacent structures. The mass was covered by omentum. The distal portion of the ascending colon seemed to be adherent to the transverse colon. The adhesions were separated without much difficulty, and a small opening was found in this inflammatory mass from which thick, greenish pus escaped. The appendix was retrocecal and did not show evidence of acute inflammation. It was removed in the usual manner. The abdomen was closed in layers with two cigaret wicks.

The patient made an uneventful convalescence. There was a purulent discharge from the abdominal sinus which eventually cleared up, and the patient was discharged well, eighteen days after operation. The wound was well healed throughout. The patient was advised to come back for further x-ray study, but he did not return to the hospital until Dec. 14, 1926.

3 cm. thick, representing a fecal fistula. The mucosa was thick, almost gangrenous about the opening.

On the ascending colon, distal to the perforation and under the site of the pocket was a shallow ulcer 1.5 by 1 cm. The base of this ulcer rested on surrounding fatty and scar tissue. Four other smaller ulcers were present, 1 cm.,



Fig. 2 (case 1).—A indicates the perforation on the ascending colon; the barium can be seen escaping in a small amount. The roentgenogram was taken following a barium enema.

4 cm. and 1 cm. in diameter, occurring at intervals of about 1.5 cm. The ulcers were pale, the edges flush with the surrounding mucosa. No communication could be found between the base of the ulcer and the surrounding scar tissue.

Microscopic examination of the ulcers showed the base made up of fibroblastic tissue which extended almost to the surface. The amount of granulation tissue was

that the entire colon was practically empty, except for a small amount of barium in the distal portion of the colon. The region of the gallbladder did not show any evidence of stones.

The nonfilling, the irregularity and the hypermotility of the colon suggested a lesion in the cecum, which I believed would be revealed after x-ray examination made after a barium enema.

The patient's temperature gradually rose and the pulse rate increased. Pain was becoming worse and the mass was growing larger. Operation was advised on August 25, ten days after admission. The results of the urinalysis were negative, and the white blood count was 13,150. The Wassermann reaction of the blood was negative.

Operation—August 25: A right rectus incision, 4 inches (10.16 cm.) long, was made over the mass under ether anesthesia. On opening the peritoneal cavity, a large amount of a thick, greenish-yellow, foul smelling, pus escaped. Exploration revealed a large abscess cavity between the ascending colon and the lateral abdominal wall. There were many pockets which were freed so that one large abscess cavity resulted. The wound was closed in layers with two cigaret wicks and one rubber tube drain. On account of the severe inflammatory reaction and the large amount of pus in the abscess cavity, nothing further was done. Swabs from the abscess at the time of operation showed colon bacilli and a few short chained streptococcus.

The patient made an uneventful convalescence from the immediate effects of the operation. A considerable amount of pus drained until the sixth day when he developed a fecal fistula. On September 8, his head blocks were removed and he was taken off the Fowler's position; the temperature and pulse were normal. Fecal matter was still draining. On September 12, there was a marked inflammatory reaction around the edges of the wound. The temperature and pulse rate were normal. On September 20, the wound stopped draining. There was a sudden rise in temperature and pain was felt in the right side. Flaxseed poultices were applied and the wound began to drain again, but from that time on the patient became progressively worse and died on October 14, seven weeks after operation.

Postmortem Examination.—A large abscess was found in the right upper quadrant of the abdomen. The lowest portion of the right lobe of the liver formed the roof of the abscess cavity; the hepatic flexure, the medial wall, and the abdominal wall, the lateral wall. That portion of the liver which formed the roof of the abscess was gangrenous and necrotic. On the ascending colon near the hepatic flexure, there was a large perforation.

Pathologic Report.—Oct. 14, 1927: The specimen consisted of 5.5 cm. of terminal ileum, cecum, ascending colon with a portion of transverse colon, the whole measuring 30 cm. in length. The external surface of the cecum and the ascending colon was covered by a mass of densely adherent mesentery and scar tissue. At the hepatic flexure, this mass of adhesions was separated to form the wall of a pocket, roughly 7 cm. in diameter. A loop of jejunum was bound to the outer surface of the pocket by dense scar tissue. The wall of the pocket was made up of fibrous tissue 3 mm. thick, lined by a greenish, necrotic membrane. Beyond the pocket, the scar tissue stopped abruptly. A portion of omentum was adherent to the transverse colon. The adhesions were readily broken.

When the intestine was laid open, nothing remarkable was found in the ileum and jejunum. The cecum was lined by a reddish thickened mucosa. The wall of the ascending colon was thickened and fibrous and showed an irregular opening

Pathologic Report.—A small piece of omental tissue the size of a lima bean was examined. Gross examination showed that it was hemorrhagic, fat tissue. The tube was congested, thickened and showed fibrous adhesions. The cyst was the size of an orange, containing clear contents. The vermiform appendix, 6 cm.

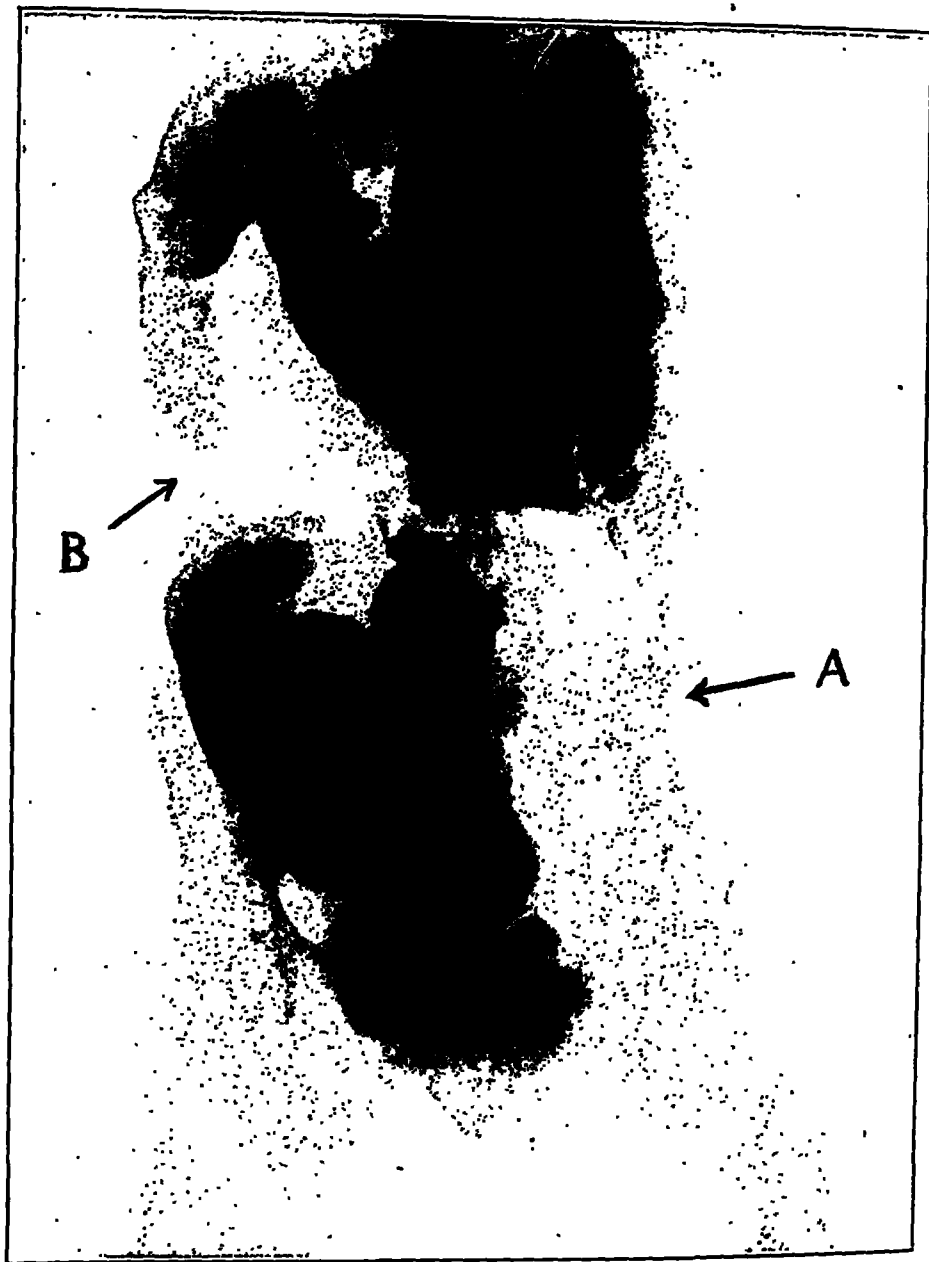


Fig. 3 (case 2).—*A* indicates the cecum, showing the filling defect three weeks after operation. *B* shows the spasm of the descending colon opposite the site of the lesion. This observation has been stressed by Carmen and others. (Roentgen-ray examination five years later showed a normal cecum.)

in length, did not show any acute signs of inflammation. Microscopic examination of omentum revealed some hemorrhage into the adipose tissue, with a marked polymorphonuclear leukocyte infiltration.

small. A cellular exudate of lymphoid, plasma and polymorphonuclear cells, relatively small in amount, was present. The surface was covered by detritus. There was a marked increase in connective tissue beneath the ulcer, associated with atrophy and disappearance of muscle fibers and extending into surrounding fatty tissue. Large collections of lymphoid and plasma cells were present and a few polymorphonuclears.

Following the patient's death, the x-ray films were again studied. From the last x-ray examination, it now seemed rather evident that there was a small perforation in the distal portion of the ascending colon through which a small amount of barium could be seen escaping from the lumen of the bowel. This was overlooked prior to the operation. However, had this complication been noted, I hardly think that anything else could have been done for this man in the presence of the severe inflammatory reaction and the collection of pus in the abscess cavity. It seemed to me that proper drainage of the abscess was sufficient treatment. The fact that the fecal fistula was established and that the temperature returned to normal, would seem as though the abscess cavity had been properly drained and that there were no fecal contents remaining within the abdominal cavity. It is possible that there was another abscess which did not drain sufficiently and which caused necrosis of the liver, which ultimately resulted in the patient's death.

CASE 2.—History.—Miss M. G., aged 23, entered the surgical service of the Beth Israel Hospital on Feb. 23, 1923, with a complaint of severe pain in right lower quadrant. The onset of the condition began two days previously. At first, pain was generalized, then it seemed to localize itself in right lower quadrant. She vomited several times during the day of entrance. There had never been any abdominal pain previously. There was no blood in the vomitus, and the patient had never noticed any blood in the stools. Cough or hemoptysis was not noted. The menstrual history and the results of the urinalysis were negative. The leukocytosis was 13,000. The family history and past history were negative.

Physical Examination.—The patient was a well developed and well nourished young woman, lying in bed complaining of severe pain in right lower quadrant. The temperature was 99 F., the pulse rate, 90. There was nothing else of note except for the abdominal examination which revealed marked tenderness in the right lower quadrant with spasm of the muscles over this region. A definite tumor or mass could not be felt. Maximum tenderness was elicited over McBurney's point. Other than this, the abdomen was soft and tympanitic. A provisional diagnosis of acute appendicitis was made, and immediate operation was advised.

Operation.—The operation was performed under ether anesthesia on the night of entrance to the hospital. A right rectus incision was made. The appendix appeared normal. On the anterior lateral surface of the cecum, there could be seen and felt an indurated, inflamed, hard mass over which some omentum adhered. The omentum was separated from the cecum, and a piece covering this mass was excised, revealing what apparently was the base of an ulcer about the size of a quarter. There was no evidence of perforation. The ulcer was round and hard, resembling a callous peptic ulcer. Three mattress sutures of silk were placed through the serosa about the ulcer and it was covered with omentum. There was no evidence of tuberculosis as far as could be seen. A simple cyst of the right ovary about the size of an orange, together with the right tube, was also excised. The abdomen was then closed in layers in the usual manner. The patient made an uneventful convalescence and was discharged well in fourteen days.

half dollar on the right lateral and posterior wall of the rectum about 6 inches from the anus. In the center of the ulcer a bleeding point could be seen from which this profuse hemorrhage apparently came. The ulcer was packed with iodoform gauze, and the patient returned to bed in good condition. On April 9, the iodoform gauze was removed from the rectum. The patient never showed any signs of bleeding from the rectum since and was discharged well on June 12.

The results of the examination of the stool were negative. The patient was kept in the hospital until this time on account of the acute arthritis of the right ankle, which eventually disappeared. The results of the urinalysis were always negative. On May 25, the white blood count was 8,600; the red blood count, 4,252,000; polymorphonuclear neutrophils, 68 per cent, lymphocytes, 22 per cent, and large mononuclears, 9 per cent.

On March 28, 1928, the patient reported by letter that she had never had any diarrhea or bleeding from the rectum since she left the hospital. She has enjoyed perfect health and has since given birth to another child.

On April 16, 1928, at my request, the patient returned for a roentgen-ray examination of the colon. The following report was made: "The roentgen examination of Mrs. S. B., was made on April 16, 1928. Part examined: Colon

TABLE 2.—*Age and Sex Incidence*

| Ages | Number of Females | Number of Males |
|---|----------------------|--------------------|
| 15-20..... | 2 | None |
| 20-30..... | 4 | 4 |
| 30-40..... | None | 4 |
| 40-50..... | 8 | 8 |
| 50-60..... | 1 | 7 |
| 60-70..... | 1 | 5 |
| 70-80..... | 2 | 2 |
| No age specified, 5; no age or sex specified, 2 | | |

(enema). The observations are as follows: The examination with an opaque enema shows the entire colon well filled and regular in contour with normal haustration throughout. No abnormalities could be noted."

AGE AND SEX

In this series of fifty-three cases, there were thirty-four males and seventeen females; in two cases the sex was not specified. One is immediately impressed with the fact that there are twice as many males as females. Apparently this seems to be a disease in which the male is more prone to be stricken than the female. The same observation has been made by many investigators regarding peptic ulcer.

The youngest female was 18 years of age, and the oldest 80; the youngest male was 20, and the oldest, 72. The average age for the group was 41.25 per cent years; for males, it was 43.5 per cent years, and for females, 41.06 per cent years, making the average age of both sexes about the same. Among the males, there was no age specified in three cases, and among the females, no age specified in two cases. Among the males, the greatest incidence occurred between the ages of 40 and 50; then 50 and 60, and then 60 and 70. Among the females,

X-Ray Examination.—X-ray examination made three days before the patient was discharged from the hospital showed that the stomach was orthotonic with normal peristalsis; the outlines of the greater and lesser curvatures were regular; the duodenum was displaced toward the lesser curvature. Examination made three hours after a barium meal showed the head of the meal in the small bowel. The stomach was empty. Examination made six hours after the meal showed the head of the meal in the terminal ileum. This marked delay of barium entering the cecum was probably due to adhesions. Twenty-four hours after a barium meal, examination showed the height of the meal in the ampulla. The cecum and the ascending colon still contained barium. A barium enema was given. The cecum was irregularly filled. The condition at the ileocecal region was pathologic and was probably due to adhesions.

At my request, the patient returned almost five years after the operation for reexamination. She said that she was feeling well since operation. She did not feel any pain. Her appetite was good and bowel movements occurred daily without the aid of cathartics. The report of the x-ray examination was as follows: "The roentgen examination of Miss M. G., was made on December 10, 1927. Part radiographed:—Colon. The findings are as follows:—The examination of the colon with opaque enema shows the entire colon well filled, regular in contour, but rather atonic. The cecum is well filled. No abnormalities could be noted."

CASE 3.—History.—Mrs. S. B., aged 32, married, entered the surgical service of the Beth Israel Hospital on March 26, 1922, complaining of bleeding from the rectum. Seven weeks before entrance, she noticed the bleeding after a bowel movement. The stool was rather large and bright red. There was a slight pain in the left lower quadrant which came on just before defecation. This pain radiated downward to the anal orifice. Since then, there had been three attacks similar to the previous one, with a considerable loss of blood each time. Diarrhea did not occur at any time, nor was there any mucus in the stools. The patient was rather constipated. Her appetite was good and she was not troubled with nausea or vomiting. Dysuria or hematuria were not noted. The family history was unimportant. The past history showed that she had had gonorrhea four years ago, but had not had any operations. Her husband was living and well; there was one child, also living and well. There had not been any miscarriages.

Physical Examination.—The patient was a well developed and well nourished young woman, lying in bed complaining of general weakness and pain in left lower quadrant. The skin was clear and of good color. There was nothing else of note except for the abdominal examination which revealed a soft and tympanitic region, although no mass or organs were felt. There was slight tenderness and resistance in the left lower quadrant.

Course.—On March 28, the patient had two loose, bloody stools. Considerable pain was felt in the left lower quadrant. On April 3, she developed an acute arthritis of the right ankle. On April 6, she had a profuse hemorrhage from the rectum. She immediately went into collapse and became extremely pale; the mucous membranes were blanched, and she complained of air hunger. The pulse rate was 150 and barely perceptible. The blood pressure had fallen to 60 systolic, 35 diastolic. A blood transfusion of 750 cc. of blood was given. Following the transfusion, the pulse rate came down to 120 and the blood pressure rose to 90 systolic and 60 diastolic. Three hours after the transfusion, the pulse rate was still 120; the blood pressure had increased to 100 systolic and 50 diastolic.

On April 7, the patient was still bleeding from the rectum in small amounts. Sigmoidoscopy revealed a large, round, circumscribed ulcer about the size of a

Cruviellhier,³ in his "Atlas of Pathologic Anatomy," expresses the opinion that the extremity of the intestine may be the seat of a simple ulcer similar to that of the stomach and duodenum.

It would seem that simple ulcer of the colon must be a manifestation of the same general disease as peptic ulcer, if there is a common etiologic factor in the production of these lesions on the various segments of the gastro-intestinal tract. This fact is particularly impressive since ulcer of the intestine is found not infrequently in association with ulcer of the stomach.

It is not unusual to find multiple ulcers of the duodenum and stomach in the same patient; there are numerous cases recorded that prove this. Recently Pickhardt¹⁰ reported a case in which there were several ulcers in the stomach and duodenum, two of which, one in the stomach and one in the duodenum, had perforated. The fact that one is ready to accept the etiology as being the same when the lesion occurs both in the stomach and duodenum, is sufficient reason to accept the same etiologic factor, even though the lesion is farther down the intestinal tract. If one may correlate ulcer of the stomach with ulcer on any other part of the intestinal tract as having a common etiology, it is obvious that there may be a healed ulcer of the stomach and an active ulcer on the colon, or, from the same cause, a simple ulcer of the colon may exist alone. If ulcer of the colon and peptic ulcer are to be considered as having common etiology, the various theories that have been advanced for peptic ulcer must be taken up.

The theories that have been advanced regarding the initial cause of peptic ulcer may be classified according to whether or not the initial lesion is regarded as inflammatory, neurogenic, circulatory, bacterial, toxic, digestive or mechanical. The symptoms and the pathologic histology would seem to indicate that practically all of these theories might apply to ulcer of the colon. There are certain theories, however, that seem to explain the etiology more than the others.

The outstanding symptom seems to be constipation, of which there are twenty-one cases; constipation was not present in five cases, and in twenty-seven cases, it was not recorded. One must take into consideration that some of the early case reports were rather incomplete, and it is possible that in the twenty-seven cases in which constipation was not mentioned that there might have been many in which constipation was present. What rôle then can constipation play in the etiology of this condition? This would necessarily bring it under the head of the mechanical theory, either direct or indirect. This view is held by many observers (Quenu and Duval,⁴ Soupault,⁵ Delafield and Prudden¹¹). Under this

10. Pickhardt, O. C.: *Ann. Surg.* 87:143, 1928.

11. Delafield and Prudden: *Textbook of Pathology*, ed. 12. New York, William Wood & Company, 1923, p. 775.

the greatest number occurred between the ages of 20 and 30, then between 40 and 50. It would seem from this study, that the average age is the same for males and females and that it is not essentially a disease of the old.

ETIOLOGY AND PATHOGENESIS

Many observers are of the opinion that simple ulcers may occur in any part of the gastro-intestinal tract, and aside from ulcers of the stomach and duodenum, there are many cases reported of ulcers of the esophagus, the jejunum, the ileum and of the various segments of the colon. Bolton,⁶ in his book on "Ulcer of the Stomach," said:

It is not uncommon to find ulcers in other portions of the alimentary canal in association with gastric ulcer. Such an association is commoner in the case of ulcers of obviously infective origin, but also sometimes occurs in the simple, acute gastric ulcer. Such acute ulcers are found in the duodenum, esophagus, lower end of ileum and the colon.

In his series of twenty-four cases of ulcer of the stomach, additional ulcers in the same patient were found as follows: in the duodenum and stomach, fifteen cases; in the esophagus and stomach, four cases; in the ileum and stomach, three cases; in the stomach, two cases. In the present series which was studied, there was found four cases of ulcer of the colon in association with ulcer of the stomach (cases 4, 7, 46 and a case reported by Chrostek quoted by Quenu and Duval⁴), and two cases of ulcer of the colon in association with ulcer of the ileum (cases 2 and 12). Combes⁷ has collected a series of thirty-six cases of simple ulcer occurring on the small and large bowel, divided as follows: seven in the jejunum, twelve in the ileum, five in the cecum, six in the colon, three in the sigmoid and three in the rectum. Gandy⁸ studied a series of fifteen cases, divided as follows: end of the duodenum, one; jejunum, two; ileum, seven; cecum, two; hepatic flexure, one, and sigmoid, two. Vidal,⁹ writing on "Ulcers of the Rectum," states: "Simple ulcers may be found throughout the whole length of the large intestine and even in the small intestine and that he has seen a few cases of chronic ulcers of the rectum." When the ulcer was single, he has only found it posteriorly. One of his patients, a man, aged 40, had symptoms of a simple ulcer of the stomach, and he believed that the ulcer of the rectum was of the same nature.

6. Bolton, C.: *Ulcer of the Stomach*. London, Edward Arnold, 1913, p. 35-35.

7. Combes, C.: *Simple Ulcer of the Intestine*, Thesis, Toulouse, 1897.

8. Gandy, C.: *Hemorrhagic Necrosis of Toxemia and Simple Ulcer*, Thesis, Paris, 1899.

9. Vidal, E.: Rectum in "*Dictionnaire encyclopedique des sciences medicales*," 1874-1881, vol. 2, pp. 678-690.

the feces may pass into the peritoneal cavity; or the perforations may be partly closed by adhesions, and abscesses or sinuses into the surrounding soft parts may be formed.

The question arises as to whether a catarrhal inflammation of the cecum or colon is primary, and ulceration a secondary manifestation. A controversy has existed for many years in regard to chronic gastritis associated with gastric ulcer. It has been held by some authors that ulcer was secondary to a chronic gastritis. I feel that it is the popular belief that a chronic gastritis is associated with, and probably secondary to, the ulcer. It would seem logical that the same condition exists in the cecum or in other parts of the colon. An ulcer being present, it may follow that secondary inflammation, either of a mild or severe character, may ensue.

According to Kocher,¹⁵ the distention as a result of constipation, obstruction or impaction of feces produces a venous stasis at first in the corresponding segment of the mesenteric artery; ecchymosis follows, then there is a desquamation of the poorly nourished epithelium, and a superficial necrosis of the mucosa is produced. As a result of the experiments of von Greyerz and von Schimodeira,¹⁶ there is a diminution in the arterial blood flow soon after distention occurs. The intestine becomes pale, and ulcers may appear even at this stage. After the distention is released, the intestine becomes deep red; a sign of venous stasis. As experimental ulcers occur as early as four or five days following distention with air, they feel that through venous stasis as a result of distention, nutritional disturbances occur in the intestinal wall, producing ulcers. Kocher and Prutz¹⁷ consider venous stasis and its resulting thrombus formation the essential cause for the formation of these ulcers. According to Rosenheim,¹⁸ the successive stages of ulceration are produced as follows: Intestinal stasis, progressive accumulation and more or less hardening of the contents, then fermentation; constant increase in the number and virulence of the bacteria, chronic inflammatory process, disorders of nutrition and ulcerating lesions. These are the theories of constipation as a mechanical factor: erosion by direct trauma, such as fecaloma, fruit seeds, etc., on the one hand, and the other, distention, due to overloading of the bowel, atony, or obstruction due to impacted feces.

The mechanical theory alone hardly seems to explain the etiology of this lesion, with constipation so universal and widespread. It would seem as though ulcer would be a much more common condition. It cer-

15. Kocher: *Deutsche Ztschr. f. Chir.*, 1877, vol. 5.

16. Von Greyerz and von Schimodeira: *Beitr. z. Chir.* 22:229, 1911.

17. Kocher and Prutz: *Arch. f. klin. Chir.*, 1900, vol. 60.

18. Rosenheim: *Ztschr. f. klin. Med.* 54:475, 1904.

theory, there could be produced the so-called stercoral or decubitus ulcer (case 49). "This type ulcer results in cases of obstipation from a crack or fissure in the mucosa which becomes infected and by extension develops into an ulceration" (Rankin¹²). According to Lyon and Bartle,¹³ stercoral or decubital ulcers are mostly confined to elderly persons, and frequently to bedridden patients. "Through lack of the proper nourishment of the body, the coils of the intestines are not changed in their position sufficiently to aid the weakened bowel musculature to pass on its contents completely enough and stagnation occurs. Hardened masses of feces form in the colon and become agglutinated to the mucosa and when they are eventually pushed along through purging, or what not, ulceration quickly follows through secondary infection, attacking the denuded bowel wall. Perforation may take place."¹³ This may explain certain ulcers in the rectum or in the sigmoid where the fecal mass may become exceedingly hard, but this can hardly be true in the cecum and ascending colon where the contents are normally fluid, and the patients in this series were not really old, with the possible exception of case 49.

Erosions, fissures and cracks might be caused by foreign bodies such as fruit pits and seeds (case 1). In this case, there was an obstruction due to an ulcer and the foreign bodies may have been lodged at the constriction later, making the occlusion complete.

Stengel and Fox¹⁴ describe ulceration of the cecum in the following manner: "Typhilitis or cecitis may be due to irritation of the intestinal contents in consequence of constipation (stercoral typhilitis)." Typhilitis is probably generally of the simple catarrhal variety, but in obstinate constipation or obstruction of the colon, ulceration may occur. Perforations or extension to the surrounding tissues is the rarest of all consequences. Usually the latter is secondary to the inflammation of the vermiform appendix. Catarrhal inflammation of the cecum, according to Delafield and Prudden,¹¹ is not uncommon. It is usually produced by an habitual accumulation of feces in this part of the intestine. The course of the inflammation is usually chronic but marked by acute exacerbations. At first, the mucous membrane undergoes ordinary changes of chronic catarrhal inflammation. To this may succeed a slow suppurative inflammation which extends through the wall of the intestine and gives rise to ulcers and perforations. Through these perforations,

12. Rankin: *Surgery of Colon*, New York, D. Appleton & Company, 1926, p. 104.

13. Lyon and Bartle: *Tice Practice of Medicine*, Hagerstown, Md., W. F. Prior Company, 1924, vol. 7, p. 615.

14. Stengel and Fox: *Textbook of Pathology*, ed. 6, Philadelphia, W. B. Saunders Company, 1915, p. 636.

sclerosis, but no endarteritis. The capillaries were dilated and there was a diffuse hemorrhagic infiltration. Arteriosclerosis can produce infarcts and thrombi, lesions effecting a small portion of the colon or a large segment of the colon by cutting off the blood supply. Quenu and Duval⁴ feel that the thrombosing endarteritis existed in the region of the ulcer in case 26. Lyon and Bartle¹⁸ describe a thrombotic and embolic ulceration. They say: "Any part of the gastro-intestinal tract may be involved by this type of lesion, but it is seen more usually in the jejunum, ileum and colon."

Boss²¹ holds that ulcers occur, as a rule, not as a primary lesion, but as a secondary manifestation, due to embolism or thrombosis of the arteries of the mesentery.

PATHOLOGY

Simple ulcer of the colon may be situated on any segment of the large intestine as shown in table 3.

The lesion may occur as a single ulcer or may be multiple. In thirty-seven cases, the ulcer occurred as a single lesion, and in sixteen cases

TABLE 3.—*Locations of Ulcer of the Colon*

| | | | |
|--------------------------------|----|-----------------------|----|
| Cecum..... | 15 | Splenic flexure..... | 5 |
| Ascending colon..... | 12 | Descending colon..... | 2 |
| Ascending colon and cecum..... | 1 | Sigmoid..... | 11 |
| Hepatic flexure..... | 8 | Rectum..... | 4 |
| Transverse colon..... | 0 | | |

they were multiple. When the ulcers were multiple, they were usually close to each other and there were never more than six. The lesion occurred most often on the cecum. The right half of the large bowel seemed to be a more frequent seat than the left, occurring in the right in thirty-one cases and on the left in twenty-two cases. This seems rather hard to explain since, as I have stated elsewhere, the contents of the cecum are normally fluid.¹² Since there were eleven cases with ulceration, either single or multiple, on the sigmoid, the question naturally arises as to whether these lesions were not diverticulitis or diverticulosis as the latter condition occurs so frequently on this portion of the colon. As these cases were all studied at postmortem examination or at operation, it seems that this question could be well ruled out. In a study of 118 patients who had diverticulitis, Judd and Pollock²² found that there was no demonstrable narrowing of the lumen of the colon below the site of the diverticula, and furthermore, it is rather unusual to find diverticula in a colon which is markedly obstructed. It is interesting to note

21. Boss, W.: Perforated Ulcer of the Large Intestine, *Beitr. z. klin. Chir.* 140:40, 1927.

22. Judd and Pollock: *Ann. Surg.* 80:425, 1924.

tainly would not be considered that constipation, directly or indirectly, could cause simple ulcer of the small intestine. The same holds true of foreign bodies such as fruit pits, seeds, etc. Frequently, one sees patients who have swallowed foreign bodies which either pass through the gastro-intestinal tract or are removed surgically; the formation of an ulcer, as a result, is rare. It would seem that the foreign bodies are immediately enveloped by the soft fecal mass, and unless the object is a large one, its hard or rough edges seldom come in contact with the wall of the bowel. The theory advanced that venous stasis is a result of distention due to constipation could not explain the etiology in all cases. It does not seem that the etiology of simple ulcer of the colon can be any more explained than the etiology of peptic ulcer, and since I feel that simple ulcer is a manifestation of a general pathologic condition as gastric ulcer is, venous stasis as a result of a general condition such as a toxemia, regardless of its origin, may play an important rôle in the etiology, but not as a result of distention due to constipation.

In an exhaustive study of ulcerations of the gastro-intestinal tract, Gandy⁸ came to the conclusion that simple ulcer of any part of the digestive tract is a manifestation of a general toxemia either of infectious or other origin. The toxemia produces an acute hemorrhagic necrosis by way of the blood stream due to hemorrhagic infarct; then follows sloughing, hemorrhagic erosion, ulceration of the mucosa, and finally, a deep ulceration. Rosenow strongly advances the bacterial theory based on the specific affinity of certain organisms for certain parts of the digestive tract. Rosenow, according to Mayo,¹⁹ maintains that certain forms of bacteria injected through the blood stream cause ulcer of the bowel, especially of the cecum. Other forms cause ulceration in the alkaline small intestine or in the acid stomach. Dickinson² believes the infection takes place in the adenoid tissue of the cecum first and then extends to the mucosa giving rise to ulceration. Intestinal parasites may be an etiologic factor as described in case 48. Stahr²⁰ studied several cases in which he felt that the parasites were the causative factors in the production of simple ulcer of both the large and small bowel.

Under the circulatory theory, one must consider diseases of the vessel walls, such as atheroma and endarteritis obliterans. The idea that ulcer depends on diseased conditions of the blood vessel is supported by the observations in a few cases. Cases 21, 24 and 41 showed these vascular lesions. Cases 21 and 24 showed arteritis in the vicinity of the ulcer and the vessel filled with coagulated blood. Case 41 showed a perivascular

19. Mayo, C., H.: Discussion of paper by G. K. Dickinson, J. A. M. A. 78: 1792 (June 10).

20. Stahr, H.: Intestinal Tumors in Children Caused by Trichocephalus, Deutsche med. Wchnschr. 48:1274 (Sept.) 1922.

desac. The edges were infiltrated and its appearance was that of a perforated ulcer of the stomach. The stomach, small and large intestines were opened. The mucosa of the entire digestive tract was normal.

CASE 45.—Autopsy was not performed. Operation revealed fecal material in the abdomen and a perforation of the sigmoid. The walls of the colon were described as rotten, and they only tore on attempts to suture. The author was unable to get a clear idea of the abdominal condition, but thinks the perforation probably resulted from thrombosis. Evidence in favor of stercoral or foreign body was scanty.

CASE 49.—Postmortem examination showed an ulcer in the transition of the rectum into the sigmoid flexure of the colon. Rupture was due to a so-called decubitus ulcer. The perforation orifice was found to contain a hard fecal mass.

CASE 50.—In the lower portion of the sigmoid there was a perforating ulcer the size of a bean, from which feces were discharged. The tissue in the vicinity of the ulcer was infiltrated, but not reddened. The ulcer was closed by five longitudinal catgut sutures; two rows were made. Sigmoidoscopy four weeks after operation showed the mucosa normal for 22 cm. Analysis of the foregoing eleven cases would rather tend to prove that the lesions were not due to diverticulitis.

Diverticulitis of the right half of the colon is rather a rare condition. In a study of twenty-seven cases, Giffen²⁴ found diverticulitis situated on the various segments of the colon as follows: Hepatic flexure, one; transverse colon, one; sigmoid, twenty-two; rectum, two, and anal ring one.

The ulcer may be the size of a pea or the size of a dollar. There are all variations in sizes between the two mentioned. They may be annular, or their long axis may be parallel with the long axis of the intestine. The description of the lesion in the various case reports differ. In some cases the ulcer is described as oval, round, irregular with sharply cut edges, circular, or they may appear to be punched out. The mucosa around the ulcer grossly appears to be normal and when the ulcers are multiple the mucous membrane between them is also normal, but, occasionally, there may be a secondary inflammation of the mucosa. There may be a chronic, diffuse, hypertrophy of the intestinal wall. The ulcer may be hard, indurated and resemble gastric ulcer. The base has been described as being yellow, gray or white. The depth of the ulcer is variable; sometimes it is shallow, involving the mucosa and submucosa alone or the muscle layer or the serosa may form the base of the ulcer. Often there is a marked overgrowth of connective and inflammatory tissue which, in the process of healing, contracts and may form an annular or longitudinal constriction, producing either partial or complete obstruction. Rarely, there is hemorrhage from the ulcer. Severe

24. Giffen: The Diagnosis of Diverticulitis of the Large Bowel, J. A. M. A. 59:864 (Sept. 14) 1912.

that in the group of cases studied for ulcer the lesion tended to cause obstruction by a healed or healing stenosing cicatrix, while in diverticulitis there was no obstruction. In this group of patients obstruction was noted in ten cases. Hanseman²⁸ noted that false diverticula usually occur and are in close relationship to the blood vessels entering and leaving the intestine along the mesenteric border. This was not the case in this study; the ulcers usually occurred on the free border or anterior surface of the bowel, with the exception of case 17. A brief résumé of the gross lesion as studied by postmortem examination or at operation of ulcers of the sigmoid follows:

CASE 5.—Postmortem examination showed that the proximal part of the colon was tremendously distended, while the rectum was much smaller. On the lower portion of the sigmoid there was a hard, annular stricture. It was so narrow that a small pin could hardly pass through it. The intestine above the stricture was covered with feces. The stricture was formed by an ulcer, the size of a 5 franc piece. The base was narrow and the edges raw, thickened and hypertrophied. Cancer could not be detected. The patient died of intestinal obstruction.

CASE 8.—Postmortem examination showed six ulcers of the sigmoid. The ulcers were oval, resembling button holes and were all about the same size, and had the appearance as if the intestine was punched out. A certain number were perforated.

CASE 14.—Postmortem examination showed an oval perforation, 5 cm. wide and 1 cm. long, on the middle part of the sigmoid. The edges were sharp and sclerotic. The mucosa had disappeared around the perforation.

CASE 15.—Postmortem examination showed a perforating ulcer with sloping edges in the lowest portion of the sigmoid flexure. It opened into the abdominal cavity. There was a second ulcer beside it, which was ready to perforate. Its border was grayish.

CASE 24.—Postmortem examination showed a linear tear on the sigmoid about 2 cm. long and surrounded by a small layer of fibrin. On opening the colon, ulcerations were found on the mucosa. One of these ulcers was deep, almost annular, and had perpendicular edges. The linear perforation already described was found to be at the base of this ulcer.

CASE 25.—Postmortem examination was not made in this case, as the patient was cured following operation, and the lesion was not visualized, although the diagnosis of perforating ulcer of the sigmoid was made (see case reports).

CASE 36.—Autopsy was not performed. Operation revealed a perforation the size of a 50 centime piece on the anterior surface of the sigmoid. The edges were slightly indurated for a short distance, and beyond the induration, the mucosa of the colon was apparently normal. The edges of the perforation were resected, and the loss of substance was sutured in two layers. Although the peritoneum and the intestine did not appear to be inflamed, extensive drainage was instituted on account of a large amount of feces in the abdomen. The patient made a good recovery from this operation.

CASE 39.—Postmortem examination showed a small, round hole in the sigmoid from about 3 to 5 cm. in diameter, and about 12 cm. above Douglas' cul-

23. Hanseman, D.: Arch. f. path. Anat. 144:400, 1896.

hemorrhage has occurred, but more often when the lesion is in the rectum, due to erosion of a blood vessel (cases 26, 47, 49 and my case 3).

In all cases, the initial lesion is acute, and an acute ulcer results. This ulcer may heal rapidly, but, on the other hand, it may extend, while a secondary inflammatory thickening occurs, corresponding in degree to the chronicity of the ulcer. A chronic ulcer, which is produced in this way, may likewise continue extending, so that a description of the ulcerative process comprises not only that of the formation of the initial lesion, but also that of the extension of acute and chronic ulcer.

However, the ulcer may continue as a chronic simple latent ulcer, giving rise to mild abdominal symptoms or, as stated before, may heal. The opposite course is perforation. From a study of this series of cases, it would seem that simple ulcer of the colon was rather prone to perforate; however, it is impossible to make this a definite statement since, in the majority of the cases studied, the diagnosis was only made when perforation occurred and it is likely that the simple latent ulcers go unrecognized. In this study of fifty-three cases, forty-two ulcers perforated and eleven did not perforate. The perforation is generally in the center of the ulcer which may be small or large. The omentum or a loop of adjacent bowel may tend to wall off and form a pocket, as in my case, one with an abscess resulting; this condition occurred in twelve cases; or the contents of the colon may be expelled into the general peritoneal cavity, giving rise to general peritonitis. The localized abscess resulting from a perforation often can be felt as a distinct tumor through the abdominal wall. The pus from this abscess may burrow and form sinuses into the liver, kidneys or any adjacent organ (cases 16, 17 and 18).

Vascular lesions about the ulcer, such as nonobliterative and obliterative endarteritis, thrombosis; complete obliteration by cicatricial fibrous tissue, penetrating into some of the capillaries have been described (cases 21, 24 and 26). There is an absence of epithelium and mucosa, and in some cases, of submucosa and muscularis. The layers lying underneath the destroyed ones have also lost their normal structure and given place to a cicatricial tissue, poor in cells but rather vascular. Ecot and Richard²⁵ found a direct infiltration of polymorphonuclear leukocytes and large phagocytic cells. There was also perivascular sclerosis.

Mintz²⁶ describes the serosa as considerably thickened with newly formed dilated vessels and a small round cell infiltration. He could not

25. Ecot, F. C., and Richard, A.: Perforation of a Simple Ulcer of the Ascending Colon: Microscopical Examination, *Bull. et mém. Soc. anat. de Paris* 92:138, 1922.

26. Mintz, W.: Simple Ulcer of the Colon, *Zentrabl. f. Chir.* 50:1208, 1923.

the possibility of a perforation of the colon to be considered. The same perforation may be found to be the cause of localized peritonitis in other parts of the abdominal cavity. After a negative exploration of an organ, which is believed to be diseased, the surgeon should remember that a chronic ulcer or a perforation of the large intestine may exist in patients whose past history shows nothing with the exception of constipation, and he should make a careful examination of the walls of the colon.

It is of particular importance to differentiate, during an operation, between a pseudoneoplasm due to an ulcer, carcinoma and diverticulitis, since in cancer, the most radical treatment possible should be carried out.

TREATMENT

In order to discuss the rational treatment of patients with simple ulcer of the colon, chronic latent ulcer and perforated ulcer must be considered separately. Since this lesion has never been correctly diagnosed in the unperforated state prior to operation, it seems rather difficult to advise operation for the condition, even though a correct diagnosis has been rendered. In spite of the fact that only fifty-three cases have been reported in the literature, it seems that the lesion must be much more prevalent and goes unrecognized. The number of perforations that have been reported is relatively small in number, which makes me believe that the ulcer or ulceration must heal itself spontaneously rather often. A certain number of ulcers do perforate, and therefore operation, before this accident occurs, is rather a simple procedure and may be a life saving measure if the ulcer be a perforating one. Apparently, simple suture of the serosa over the base of a shallow ulcer is sufficient treatment, as proved in case 40 and in my case 2. When the ulcer has caused definite constriction, due to a healed contracting scar, a simple plastic operation may be sufficient rather than extensive resection. If, however, the ulcer, as a result of inflammation, has produced a pseudoneoplasm protruding within the lumen of the bowel causing definite obstruction, the usual resection of that portion of the bowel must be performed. The surgical treatment for persons with simple ulcer in the unperforated state may be divided as follows: (1) for simple shallow ulcer without constriction or obstruction, simply bringing the serosa over the base of the ulcer as reinforcement is sufficient; (2) for the constricting band due to a perfectly healed ulcer, a plastic operation is sufficient; (3) for an obstructing type of ulcer with secondary inflammation, the treatment must be resection.

The treatment in cases of perforated ulcer must be immediate operation. If the perforation is immediately visualized and opens directly into the peritoneal cavity, the ideal method would be to suture the perforation

shock is present, then to be followed by the usual signs and symptoms of general peritonitis as arises following perforation of any hollow viscus.

2. Ulcer of the colon sometimes forms an intra-abdominal tumor, owing to a small perforation which causes an extensive infiltration of the abdominal wall. There is a surrounding peritoneal reaction; adhesions of the small intestine or omentum form a true tumor which can be often felt. This type usually gives rise to localized pain and rise in temperature; if it is on the right side, like appendical abscess. There were twelve cases, about 22.5 per cent, in which a definite, palpable tumor could be felt (cases 19, 21, 24, 25, 27, 28, 29, 31, 39, 40, 48 and 51, and in cases 40 and 48, the ulcer had caused an intussusception. Occasionally, these symptoms subside due to a local, natural, defense reaction. The virulence of the invading organisms is lowered. The perforation is closed over by a layer of fibrin, then layer on layer of inflammatory tissue is deposited about the localized perforation. The temperature may become normal and even the pain may disappear, and the patient believes himself to be well. The inflammatory tumor persists however, and can be easily palpated. Essentially, the symptoms of perforated ulcer simulate those of peritonitis, either local or general.

DIAGNOSIS

The diagnosis of ulcer of the colon is difficult to establish before perforation has taken place. Simple ulcer of the colon has no pathognomonic signs by which the diagnosis can be made. In not one of the cases in the series studied was the diagnosis made before perforation or operation took place, with the exception of the case in which the ulcer was located in the rectum. Constant, fixed pain, associated with constipation, should make one suspect ulcer as well as cancer in the differential diagnosis. At best, this lesion can only be suspected, and, with the aid of the x-ray, the diagnosis may be made. The sigmoidoscope and proctoscope will be of considerable assistance when the ulcer is in the rectum, or low down in the sigmoid. X-ray examination will help to rule out a diagnosis of colitis and cancer.

When the ulcer has perforated and signs of peritonitis, either local or general, have made themselves evident, the diagnosis is usually made at operation. If an abdominal tumor can be felt, together with acute inflammatory signs, perforation of an ulcer should immediately be considered. The first impression is a perforated appendix, acute cholecystitis, volvulus, strangulation or intussusception, but whatever diagnosis is made, on account of the gravity of the symptoms, operation is usually performed at once. It is then that a knowledge of ulcers of the colon appears to be particularly valuable. In fact, in a peritonitis involving the right iliac fossa, the finding of a normal appendix should cause

There were approximately twice as many cases of ulcer of the colon in males as in females. This is not a disease of old age; the average proving that it occurs before middle life.

Perforations occurred in forty-two of the fifty-three cases reported.

REPORTS OF CASES FROM THE LITERATURE

CASE 1 (Marchesseaux,²⁷ 1837).—*Perforation of Ulcer of the Rectum.*

A woman, aged 45, an alcoholic with marked constipation, died of acute peritonitis. At autopsy, a stricture was found in the upper part of the rectum. Above the stricture, many grape seeds and fruit pits were found. The stricture barely permitted the passing of one's little finger. There was a large circular ulcer on its surface about 1 inch (2.5 cm.) wide; the edges were formed by slightly swollen, pale mucosa. The base was pale and was formed by the submucous connective tissue. In the center, a small perforation was noted. The intestinal coats were only slightly thickened. There was no evidence of ulcer in any other point of the gastro-intestinal tract. All the other viscera were normal.

CASE 2 (Rogee,²⁸ 1838).—*Chronic Ulcers of the Intestine Without Tubercular Perforation.*

A woman, aged 61, with a delicate constitution, for three years had been having frequent attacks of colic accompanied by nausea and vomiting. Diarrhea had not occurred. The condition gradually disappeared. She had no primary acute infection. She suddenly had violent pains in the abdomen and died with signs of peritonitis. At autopsy, the lungs showed evidence of old healed tuberculous process in both apexes. The viscera were normal. The peritoneum showed signs of acute peritonitis. There were six narrow ulcers in the last fifth of the small intestine opposite the attachment of the mesentery. The ulcers were elongated and their great diameter was perpendicular to the axis of the intestine. The base of some of the ulcers was formed by the peritoneum only; in others the base was formed by the muscle layer, and in some the submucous connective tissue formed the base. Granulations were not seen on the surface of the ulcers. Only one ulcer in the colon, situated high up in the rectum, perforated. It presented the same characteristics as the ulcers of the small intestine, but it was round and about the size of a 2 franc piece. The mucosa of the gastro-intestinal tract was normal with the exception of the ulcers. The mesenteric glands were normal and there was no evidence of tuberculosis present.

CASE 3 (Greenhow,²⁹ 1848).—*Perforating Ulcer of the Splenic Flexure.*

A man, aged 72, had an attack of renal colic six months before consulting a physician. Examination showed a calculus in the bladder. Lithotomy was performed on November 7. On November 9, slight abdominal pain, rapid pulse and marked constipation developed. Mild mercuric chloride was given on November 10; the patient grew weaker and had diarrhea, death occurred that morning. At autopsy, the peritoneum showed signs of peritonitis. The coats of the bladder were markedly thickened. The prostate was indurated and large. A small calculus

27. Marchesseaux: Stricture of the Upper Part of the Rectum with Old Ulceration, *Bull. Soc. anat. de Paris* 12:343 (Dec.) 1837.

28. Rogee: Chronic Ulcers of the Intestine Without Tuberculosis; Perforation; Acute Peritonitis; Death, *Bull. Soc. anat. de Paris* 13:181 (Aug.) 1838.

29. Greenhow: Perforating Ulcer of the Splenic Flexure, *Path. Soc. Newcastle and Calestead*, December, 1848.

without the excision of the edges, cleansing the abdominal cavity of fecal and purulent material and establishing adequate drainage. Certainly, resection would be contraindicated in the presence of a more or less generalized peritonitis. If the perforation has been walled off and a localized abscess has developed, incision, evacuation of the abscess, suture of the perforation whenever possible, without too much manipulation, and adequate drainage would be sufficient, rather than performing a more complete and dangerous operation.

When the ulcer is sufficiently low in the rectum, cauterization and tamponade is probably enough, as in case 26. In my case 3, tamponade was enough to check the hemorrhage, and the ulcer apparently healed itself.

SUMMARY

Fifty-three cases of simple, nonspecific ulcer of the colon are reported. Fifty cases were collected from the literature and three were personal cases. There were thirty-four autopsies, one incomplete autopsy and two deaths without autopsies in this series. Fifteen patients were cured as a result of operation; two of these patients had intestinal resections performed and the resected colon was studied grossly and microscopically. The others were studied only by visualization at time of operation. In one case, it was not stated as to whether the patient survived or not.

Simple ulcer, analogous to gastric or duodenal ulcer, may occur on any part of the alimentary canal from the esophagus to the rectum. Ulcer of the colon is a distinct and definite pathologic lesion which probably occurs more frequently than is suspected; the diagnosis usually being made only when the ulcer has perforated, or during an exploratory laparotomy or at the time of a postmortem examination.

Simple ulcer of the colon is usually the cause of the so-called inflammatory tumor or pseudoneoplasm and as a result of which, intestinal obstruction is produced either by the inflammatory tumor or constriction, usually due to a healing ulcer or the cicatrix of a healed ulcer.

The etiologic factor is probably not constipation and therefore stercoral or decubital ulcers are not common. Simple ulcer of the colon is not infrequently associated with gastric or duodenal ulcer. The fact that ulcer occurring on the stomach and on the first portion of the small intestine, namely, the duodenum, is accepted as having the same etiology, it is logical to believe that ulcer of the stomach occurring with an ulcer on another segment of the gastro-intestinal tract, namely, the colon, have the same etiology. Therefore, it seems that ulcer of the colon is probably a secondary and local manifestation of a general pathologic condition as gastric ulcer, and that the same etiologic factor may be the cause of simple ulcer on any segment of the alimentary canal.

a perforation of an ulcer of the sigmoid colon was found. This ulcer communicated with a closed pocket of cellular tissue as a result of the inflammation so that the fecal contents had not escaped into the free abdominal cavity and this explains the length of his illness.

CASE 7 (Claus,³² 1856).—*Perforating Ulcer of the Descending Colon.*

A man, aged 47, had had typhoid twenty-five years previously and pneumonia fifteen years previously. On May 8, 1855, he had pneumonia again. On the seventeenth day of his illness, dyspnea increased and he had violent pains in his abdomen. He had diarrhea, followed by constipation which could not be relieved. He died two days after entering the hospital with evidence of peritonitis. At autopsy, on the lesser curvature of the stomach, an ulcer the size of a 5 centime piece was found and there were several other small ulcerations on the greater curvature. The small intestine was slightly hyperemic and contained four or five round worms. There was a rounded perforation the size of a 5 centime piece on the posterior wall of the descending colon and the edges were perpendicular. Nothing else was found in the gastro-intestinal tract. The lungs showed evidence of pneumonia.

CASE 8 (Dickinson,³³ 1867).—The patient was a woman, aged 42, who died in St. George's Hospital on Aug. 26, 1863. She said that she had had constipation and a bilious fever several months before admission. About a month before her death, she had pains in the left iliac fossa and died with symptoms of a circumscribed peritonitis. At autopsy, a cavity the size of a cocoanut was found in the left iliac fossa. This cavity was partly empty. The anterior wall of the cavity was formed by the abdominal wall and the posterior wall was formed by intestinal loops which were adherent to each other by means of solid lymphoid tissue. The cavity contained pus and feces, and communicated with the sigmoid by means of a certain number of perforating ulcers. About half a dozen ulcers were seen on opening the colon. The ulcers were oval, resembling button holes and were all about the same size. They were close together, parallel to each other and perpendicular to the long axis of the intestine. They did not present any thickening, and they had the appearance as if the intestine was punched out. The muscular layer was destroyed. There was no evidence of tuberculosis.

CASE 9 (Idem).—*Perforating Ulcers of the Descending Colon.*

The patient was a man, aged 42, who died at St. George's Hospital on Feb. 10, 1865. He had attacks of pain in the left hypochondrium for several years. These attacks have become worse recently. Pain was associated with constipation and he would be relieved by cathartics. The patient became edematous; his urine contained albumin and he had diarrhea which could not be controlled. This appeared to be the cause of his death. At autopsy, a large cavity filled with black feces was found. The cavity was made up of the diaphragm, spleen and descending colon. There were two small narrow ulcers in the upper part of the descending colon which opened into this cavity. There was no thickening of the intestinal coats. There was no other lesion present with the exception of the ulcers. These ulcers were in the form of button holes, close together, and parallel and their long diameter was perpendicular to the long axis of the intestine. No evidence of tuberculosis was found.

32. Claus, A.: Spontaneous Perforation of the Colon, Inaug. Diss., Zurich. 1856.

33. Dickinson: Perforating Ulcer of the Transverse Colon, Tr. Path. Soc. Lond. 18:101, 1867.

was found in the bladder. There was a large amount of feces in the left hypochondrium. There was a small perforation at the splenic flexure from which the intestinal contents escaped. The colon presented ulcers at a few other points. These other ulcers had almost penetrated through the entire thickness of the intestinal coats. Immediate cause of death was peritonitis due to perforation.

CASE 4 (Lebert,³⁰ 1861).—*Perforating Ulcer of the Colon.*

A man, aged 47, who had always been in good health, had sharp pains in the abdomen fifteen days before admission to the hospital. Pain was localized along the course of the colon. He became markedly distended, and later constipated. There was nausea and vomiting. On admission to the hospital, he had signs of peritonitis and died two days afterward. At autopsy, there was general peritonitis. The abdomen was filled with gas and there was a large amount of feces in the right iliac fossa. The lesser curvature of the stomach presented an ulcer about the size of a 5 centime piece, about 10 cm. from the cardia. The small intestine was normal. There was a rounded perforation a little larger than a 5 centime piece at the splenic flexure surrounded by an area of injection and false membranes. The ulcer when seen from the mucous surface showed the edges to be almost perpendicular.

CASE 5 (Idem).—*Ulcer of the Sigmoid; Intestinal Obstruction; Death.*

A man, aged 47, had always been in good general health, although he always complained of marked constipation and hemorrhoids. He continued to work until ten days before his death. At this time he began to vomit and became markedly constipated. In spite of all that could be done, the constipation persisted and his abdomen became more distended, but without pain. He was much nauseated and vomited continually until his death.

At autopsy, the abdomen was found to be markedly distended. There were only a few adhesions. The only changes were found at the lowest portion of the sigmoid. Above this point, the colon was tremendously distended while the rectum was much smaller. At this point, there was a hard annular constriction. The stricture was so narrow that a small pin could hardly be passed through. The intestine above the stricture was filled with feces. The stricture was formed by an ulcer the size of a 5 franc piece. The base was yellowish and the edges broad, thickened and hypertrophied. After careful examination with a microscope, cancer could not be detected. There was a single simple ulcer which had caused the obstruction of the intestine, by increasing hypertrophy of the intestinal walls.

CASE 6 (Dujardine,³¹ 1864).—*Perforating Ulcer of the Splenic Flexure.*

A physician, who became suddenly ill with pain on April 12, described the pain like that of a sharp blow which caused him to sit down and rest. Shortly after, he was able to walk home complaining of a pain in the left hypochondrium. His physician made a diagnosis of colitis and applied leeches which seemed to give him relief. At the end of twenty days, he was advised to go to the country for a rest. He did not improve and complained of indigestion and pain. On returning, he consulted Prof. Orsey on June 5, who made a diagnosis of tumor of the spleen or adjacent organs and advised waiting until the next day because he wished to see the color of the patient's skin before he made his final diagnosis. He had several attacks of pain with diarrhea and fever and died on June 24. At autopsy,

30. Lebert: *Perforating Ulcer of the Colon*, *Traité d'anatomie et pathologie générale et spéciale*, 1861, vol. 2, p. 206.

31. Dujardine: *Perforating Ulcer of the Splenic Flexure*, *Soc. d sc. méd. et naturelles de Bruxelles*, September 5, 1864.

any tuberculous lesions. The mucosa stopped abruptly where the ulcers commenced. The objective appearance was that of a simple ulcer. The stricture at the splenic flexure was due to the cicatrix of a healed ulcer.

CASE 13 (Choupe,³⁷ 1870).—*Simple Ulcer and Stricture of the Large Intestine.*

A man, aged 32, had colic almost continuously for two months. He vomited after every meal, and colic returned after vomiting. The vomitus and feces were black. The patient was very constipated and would go for seven or eight days without a bowel movement; this condition would be followed by diarrhea. His appetite was good. At autopsy, there was no evidence of tuberculosis. There were signs of peritonitis in the abdominal cavity. The cecum and ascending colon were enormously distended. A stricture was situated at the hepatic flexure. Palpation at this area did not show any indurated tissue. After having incised the large intestine above and through the stricture, a large ulcerated area with irregular borders was found in center of stricture. No evidence of malignancy or any other lesion was found in the gastro-intestinal tract.

CASE 14 (Demange,³⁸ 1879).—*Old Perforation of the Sigmoid Flexure, Obstructed by Epiploic Adhesions; Rupture of These Adhesions; Acute Peritonitis.*

A man, aged 72, had sharp abdominal pains one evening, and was found dead the next morning. At autopsy, generalized acute peritonitis was found. There was an oval perforation 5 mm. wide and 1 cm. long on the middle part of the sigmoid flexure. The edges were sharp and sclerosed. The mucosa had disappeared around the perforation. The base of the ulcer was occupied by epiploic masses which were adherent to the edges and which undoubtedly formed a stopper up to the time of rupture.

CASE 15 (Mickle,³⁹ 1883).—*Double Perforating Ulcer of the Sigmoid Loop of the Colon.*

A man, aged 45, had an extremely severe pain in the right iliac region near the median line after having taken a purgative. There were signs of peritonitis due to perforation. He died twenty-four and a half hours after this sudden onset. Autopsy revealed generalized peritonitis. There was a perforating ulcer with sloping edges in the lower portion of the sigmoid loop. It opened into the abdominal cavity. There was a second ulcer beside it which was ready to perforate. Its borders were grayish. There was stenosis of the mitral valve and biliary calculi, but no calculi were found in the intestine or peritoneum.

CASE 16 (Bradbury,⁴⁰ 1884).—*Ulcer of the Cecum, Complicated with Abscesses of the Liver.*

A man, aged 30, was admitted to the hospital on May 28, 1884, with a condition, the first symptoms of which appeared on April 25 and consisted of abdominal pain on the left side, chills, vomiting, diarrhea, fever and loss of weight. On admission, there was dulness over the base of the left lung. The abdomen was soft but painful in the left iliac fossa. Cough was noted. Examination did not show the presence of a rash. There was an alternation of the chills and fever. The

37. Choupe: Simple Ulcer and Stricture of the Large Intestine, *Bull. Soc. anat. de Paris* 45:322 (May) 1870.

38. Demange, E.: Old Perforation of the Sigmoid; Acute Peritonitis, *Rev. méd. de l'est*, August, 1897, p. 500.

39. Mickle: Double Perforating Ulcer of the Sigmoid, *Brit. M. J.* 1:637, 1883.

40. Bradbury: Ulcer of the Cecum, Complicated with Abscess of the Liver, *Lancet* 2:637, 1884.

CASE 10 (Robin,³⁴ 1869).—*Ulcer of the Descending Colon.*

A man, aged 66, entered the hospital on May 19, 1868. He had had gout since he was 19 years of age. On the morning of May 20, he had a severe attack of gout and there followed severe constipation for five days with slight abdominal distention. He was given a purgative, which caused one bowel movement. On May 26, the patient demanded his discharge from the hospital. This was refused on account of the increase in the abdominal distention. The constipation and distention increased. His condition became serious on May 29. There had not been any stools for several days. He now had a weak pulse, coldness of the extremities and vomiting. Galvanism was applied to the abdomen without results. It was impossible to pass an esophageal sound to the upper limit of the rectum. The patient's condition became much worse and death followed. At autopsy, the intestine protruded on opening the abdomen. The colon was distended with gas and liquid feces; its walls tore at the slightest traction. There was no evidence of peritonitis or strangulation. There was an ulcer the size of a 5 franc piece in the middle portion of the descending colon. The ulcer was of recent date. Nothing was found which could explain the arrest of the sound in the rectum. Crystals of sodium urate were found in the articulations of the toes.

CASE 11 (Costin,³⁵ 1870).—*Perforating Ulcer of the Ascending Colon.*

A man, aged 45, had had abdominal pain, constipation and slight fever. Palpation showed that the colon was filled with hard feces. Various purgatives such as castor oil, mild mercuric chloride, senna and croton oil were administered without any notable result. The patient died twelve days after he was first seen. At autopsy, the small intestines were found to be distended. There was evidence of peritonitis. There was a certain amount of exudate in the peritoneal cavity and it had a fetid odor. The right side of the omentum was gangrenous and presented small disseminated abscesses. There was an old ulcer with sharp borders on the posterior surface of the middle third of the ascending colon. It had perforated through the entire thickness of the intestinal wall. The other viscera were normal.

CASE 12 (Lepine,³⁶ 1870).—*Annular Ulcer of the Intestine; Perforation of the Small Intestine; Stricture of the Large Intestine, Autopsy.*

A woman, aged 70, died in the service of Dr. Charcot shortly after admission to the hospital. There was no clinical information. The abdomen was large, and the peritoneum was markedly injected. Several loops of intestine were covered with false membranes. The small intestine and the ascending and transverse colon were dilated, but the descending colon was of normal size. There was a stricture at the splenic flexure. The little finger could not be passed through this stricture. The intestinal walls were greatly thickened through the whole extent of the stricture. There was a round ulceration of small size a few millimeters above the stricture. The mucosa of the large intestine was normal throughout with the exception of the small ulcer. In the terminal ileum, there were six round ulcers penetrating to the muscle layer. The ulcer which was most distant from the ileocecal valve was 2 or 3 cm. in diameter, and the borders were thin. Careful examination showed that this perforation had not been artificially produced during autopsy and that it produced the terminal peritonitis. There was no evidence of

34. Robin: Ulcer of the Descending Colon, Thèse Denaire, Paris, 1869.

35. Costin, J. G.: Perforating Ulcer of the Ascending Colon, Brit. M. J. 2: 247, 1870.

36. Lepine: Perforation of the Small Intestine; Stricture of the Large Intestine, Bull. Soc. anat. de Paris 45:27 (Jan.) 1870.

There was a continuous discharge of pus from the thoracic wound. The functions of the digestive tube were perfectly regular. The cachexia increased toward the end of May, and the patient died on June 2, 1886.

Autopsy showed that the head was normal, and the pericardium was distended with about 1 pint (473.2 cc.) of clear and limpid fluid. Pericarditis was not noted. The pleura were adherent and contained a cloudy liquid rich in fibrin. Examination of the lungs showed generalized bronchopneumonia with suppuration and formation of small disseminated abscesses. The left lung was in a worse condition than the right. Peritonitis was not found in the abdomen. The ascending colon was firmly united to the liver at the hepatic flexure. It formed one of the walls of the cavity filled with pus. This suppuration extended into the right lobe of the liver, which was softened and friable. It communicated with an opening in the right flank by means of a narrow fistula situated in the posterfor axillary line between the ninth and tenth ribs. There was only a small amount of pus. The tenth rib was necrotic at the level of the sinus. On opening the ascending colon, a small ulcer the size of a pea was found. It was evidently of old formation and had perforated the wall of the intestine and opened into the area of suppuration. The ulcer was circular and had rounded edges. It did not present any trace of active evolution. There was nothing to indicate the origin of this ulcer. The rest of the digestive tract was normal. The spleen showed amyloid degeneration. The kidneys were fatty and slightly amyloid. The pelvic organs were normal.

CASE 19 (Idem).—*Ulcer of the Colon and Cecum.*

A woman, aged 49, fell from a wagon on Aug. 14, 1887. She entered the hospital on August 16 for contusions of the face and the right thigh and abdominal pains. There was no history of previous abdominal disorders. Her general condition was grave. She was constipated for six days following the accident and had continual, greenish and aqueous vomiting. She had a profuse evacuation on August 20, undoubtedly due to a purgative; her stools were fetid and liquid; the vomiting ceased; she had fever; the diarrhea persisted. Examination of the urine did not show any albumin. On August 28, a diffused swelling was found at the hepatic flexure. The patient was weak and her temperature was normal. A tumor gradually developed and became of considerable size. It was situated at the hepatic flexure of the colon. There was a gradual weakness; the stools were irregular and were dark, fetid and liquid. On September 20, she had cough, pneumonic expectoration and fine crepitant râles at both bases. The diarrhea and cachexia continued, and the patient died on October 20. At autopsy, the heart and pericardium were found to be normal. The pleurae were also normal. The right lung showed hepatization of the base and disseminated suppuration. The left lung showed generalized bronchopneumonia and the bronchi were filled with pus. Chronic generalized peritonitis was found in the abdomen; the intestinal loops were adherent to each other. There was a collection of fecal matter and pus around the cecum and ascending colon. This collection extended upward as far as the diaphragm, passing in front of the liver. The pus and feces were contained in adhesions. There was a circular ulcer at the base of the cecum opposite its peritoneal insertion. This ulcer had rounded edges and had perforated through the intestine. It did not present any sign of recent evolution. It was the size of a 3 pence piece. A second similar ulcer, twice the size of that of the cecum, was found on the anterior wall of the ascending colon about 3 inches (7.6 cm.) from the cecum. There were no signs of typhoid, dysentery or tuberculosis. The intestines were soft and were in putrefaction. The right kidney showed congenital atrophy; it was the size of the kidney of an infant, while the left kidney was twice the normal size. The other abdominal viscera were normal.

abdomen became distended and painful on June 25, and the area of dulness around the liver increased. Acute pain developed in the right flank on July 9, and there was a large pleural effusion of the right side. The patient died on July 16. Autopsy revealed the right pleura filled with yellowish pus which had a nauseating odor. There was a fistula communicating between the pleura and an abscess of the liver. The liver contained many abscesses of various sizes, the largest of which was about the size of a lemon. This was the abscess which had ruptured through the diaphragm. There was an ulcer the size of a pea in the intestine near the attachment of the appendix to the cecum. It was surrounded by congested mucosa, but there was no perforation of the wall. There was no evident cause of the ulcer; the appendix was normal. The cecum was fixed in the right iliac fossa by old adhesions. The hemorrhoidal veins and the inferior mesenteric veins were filled with clots and pus. There were no lesions in the rectum or small intestine.

CASE 17 (Oliver,⁴¹ 1895).—*Acute Perforating Ulcer of the Ascending Colon.*

At autopsy, there were two longitudinal ulcers in the colon $2\frac{1}{2}$ inches (6.27 cm.) above the ileocecal valve. The larger ulcer was about 1 inch (2.5 cm.) in diameter, while the other scarcely admitted the tip of a goose feather. The surrounding tissues appeared to be normal as well as the tissue between the two ulcers. The two perforations were of rounded form and their edges were perfectly regular. The different tunics of the intestine had undergone necrosis to an equal degree; however, the muscle layer was retracted so that there resulted a prolapse of the mucosa which appeared to be redundant.

The larger opening, seen from the outside, presented the appearance of an artificial anus while the smaller opening could scarcely be discovered because of the retraction and the elasticity of the intestinal tissue.

The ulcers were situated exactly in the middle of the posterior surface of the ascending colon. The posterior surface, which was not covered by peritoneum, was lined by the connective tissue of the fascia which filled the lumbar space and the anterior surface of the right kidney. The necrosis had gradually extended through the intestinal wall, forming a tunnel through which fecal material escaped into the areolar tissue separating the colon and the right kidney from the subadjacent tissues. The peritoneum showed only slight signs of inflammation; only the lower edge of the liver presented traces of fibrinous exudate over a limited area.

CASE 18 (Parker,⁴² 1887).—*Ulcer of the Ascending Colon.*

A girl, aged 18, entered the hospital on Sept. 16, 1885 for perityphilitis; she had been treated with rest and poultices. She improved and left the hospital in six weeks. On Dec. 24, 1885, she noticed a swelling in the right thorax redness, tension and dyspnea. The tumor increased in size; she coughed and expectorated. She returned to the hospital. The abscess was punctured on January 12, but only a half ounce (14.7868 cc.) of pus was obtained. An incision was made on January 13. The cavity was irrigated, but there was little pus. The patient's general condition improved at first and then became worse; cough, profuse expectoration, night sweats and hectic fever developed. At about the middle of February it was believed that there were signs of subacute pulmonary tuberculosis.

41. Oliver, J.: Acute Perforating Ulcer of the Ascending Colon, *Lancet* 1: 424, 1885.

42. Parker, A.: Ulcer of the Ascending Colon, *St. Barth. Hosp. Rep.* 23:213, 1887.

the cecum. The postoperative course was uneventful. The patient became cured and left the hospital on the fortieth day. He was in perfect health two and one-half months later and had gained 12 Kg. in weight.

Examination of the cecum showed that the tissue removed at operation consisted of the cecum, appendix, ascending colon, a part of the transverse colon and 2 cm. of the small intestine. The total length was 35 cm. The intestine was opened following along the external border. This incision divided a loss of substance into two almost equal parts at the level of the cecum. It was an oval ulcer with sharp outlines and the edges were about 2 mm. high. The base was indurated, pale gray and of uniform coloration. This ulcer was almost opposite the valve of Bauhin; its small vertical axis measured about 3.5 cm.; its great axis was in a transverse direction and measured 7 cm.; and the two extremities of this transverse great axis were each 1.5 cm. from the commissures of the ileocecal valve. The mucosa of the cecum was not absolutely normal; it appeared to be slightly infiltrated, and in addition, it presented white streaks which radiated from the edges of the ulcer. These streaks were almost fibrous and they flattened the folds of the mucosa, which was pink and shining. The mucous membrane of the intestine was normal in all of the other portions. The ulceration was in the middle of a large indurated plaque of almost cartilaginous hardness. This induration was situated on the antero-external and posterior walls of the cecum for a distance of about 7 cm. Its edges decreased in hardness and gradually disappeared. At the level of the induration, the intestine was considerably thickened and measured more than 1 cm. The intestine seemed to be of normal thickness in all other parts.

Microscopic examination at low magnification showed that the ulcer had destroyed the entire thickness of the glandular layer, the musculature of the mucosa and the most superficial part of the mucous membrane. The glands were increased in length about 5 cm. The connective tissue was much more dense than that of normal intestine; it formed tight, thick bundles which stained intensely with acid fuchsin. The muscular layers were hypertrophied; the internal layer measured 3 mm. and the external layer 2 mm. The serosa was also slightly thickened. Under higher magnification, it was found that in the vicinity of the ulcer the glandular layer was infiltrated in its entire thickness by a large number of embryonal cells. At certain points, these cells formed masses resting on the musculature of the mucosa. The epithelial lining cells of the intestine and those of the tubular glands appeared to be normal. The base of the ulcer was formed by the serosa; it was made up of connective tissue bundles irregularly sectioned by the ulcerative process. In the superficial parts especially, it was infiltrated by a large number of embryonal cells and at certain points there were small interstitial hemorrhages. Vascular lesions could be seen below the ulceration; certain arterioles showed obliterating endarteritis; others were thrombosed and filled with coagulated blood; finally there were larger vessels which presented slight traces of endarteritis. In many places the connective tissue around these vessels was thicker and tighter than elsewhere. The vascular lesions were far from being generalized; most of the arterioles subadjacent to the ulcer appeared to be completely normal. Sections of the colon above the ulcer showed that the coats of the intestine were normal and there were no vascular changes.

CASE 22 (Southam,⁴⁵ 1895).—*Perforating Ulcer of the Cecum.*

A man, aged 67, who had suffered from symptoms of incomplete obstruction of the intestine for several months, died suddenly a short time after admission to the

45. Southam: Perforating Ulcer of the Cecum, Brit. M. J. 1:254, 1895.

CASE 20 (Ollier,⁴³ 1892).—*Slough of the Cecum; Perforation.*

A man, aged 56, suddenly had a violent abdominal pain. There were signs of peritonitis and he died on the seventh day. Autopsy showed generalized peritonitis. There were two perforations of from 1 to 3 mm. in diameter, on the anterior surface of the cecum 2 or 3 cm. from the ileocecal valve. They were on the internal surface of the intestine in the center of a gangrenous area which was the color of dead leaves and was 5 or 6 cm. long and 1 to 1.5 cm. wide and surrounded by an area of inflammation. The rest of the intestine was normal and the appendix was intact.

CASE 21 (Morel and Secheyron,⁴⁴ 1895). *Ulcer of the Cecum; Inflammatory Pseudoneoplasm; Ileocecal Resection; Cure.*

A man, aged 46, entered the hospital on Sept. 17, 1895, for digestive disorders and progressive general weakness. He was tall and thin. On admission to the hospital, his face had an earthy tint, and his features showed a condition of general weakness. The disease began on July 14, 1895. Suddenly and without any cause, while working, he had had a severe pain in the right iliac fossa. Nevertheless, that day and the following days he had been able to continue working, but he had had almost continual pain. This pain presented exacerbations at fixed periods, coming on two hours after each meal. In the interval, there was rather a sensation of weight or heaviness at the level of the cecum, than a true pain. The digestive functions continued to be regular; there was no constipation or diarrhea. Stools were passed every day without increasing the pains and without discharge of blood and melenæ. His appetite remained excellent, but in spite of these conditions, he lost weight and strength.

From the beginning of the disease, the patient had noticed a swelling in the right iliac fossa. This swelling was situated between the anterior superior spine of the ileum and the umbilicus. Palpation was not painful, and showed an ill defined, elongated, lobulated tumor which was mobile in all directions. The dulness was not absolute on percussion. There were no adhesions to the skin. The glands in the groin were normal. In the presence of this tumor, and especially on account of the patient's straw-yellow color and earthy tint, a diagnosis was made of cancer of the cecum. The tumor seemed to be well limited, nonadherent, and surgical operation seemed to be justified. The patient was placed on a milk diet for eight days and he was given benzonaphthol to produce intestinal asepsis as much as possible. Another careful examination was made before giving the anesthetic. A small tumor could be clearly felt at the upper part of the right iliac fossa. It was mobile and the size of a small apple. It seemed to be surrounded by a sort of resistant and lobulated tissue. After the patient was under the anesthetic, it was impossible to palpate this tumor and only a diffuse swelling could be felt.

Operation was performed. Palpation of the abdomen showed a tumor which protruded into the cecum. This tumor was surrounded by an indurated zone which extended along the external wall of the cecum to 6 or 8 cm. from the valve. There was an oval, thickened plaque, about the size of a 2 franc piece, situated on the adherent border of the mesocolon 10 or 12 cm. from the valve. It was milky white. The mesenteric glands near the cecum were large and hypertrophied. The appendix was normal. The diagnosis at operation was cancer of

43. Ollier: A Case of Double Perforation of the Cecum, *Loire méd.* 11:3 (Jan. 15) 1892.

44. Morel and Secheyron: Ulcer of the Cecum: Pseudoinflammatory Neoplasm; Ileocecal Resection; Cure, *Soc. de méd. de Toulouse*, 1895.

and considerable gas escaped on opening the peritoneum. The true pelvis was filled with a cloudy, seropurulent fluid containing fibrinous false membranes. On examining the contents of the abdomen, one single loop of intestine was found to be of enormous size and was recognized to be a portion of the large intestine. It extended obliquely from the right iliac fossa to the left hypochondrium. On elevating it slightly, a linear tear about 2 cm. long and surrounded by a small layer of fibrin was found on the right lateral surface. Intestinal matter was escaping through this opening. Great difficulty was experienced in determining which portion of the large intestine was affected. However, it was evident that this distended loop was the sigmoid which had greatly increased in size and had left the true pelvis to extend into the abdomen in front of the viscera. After having extracted this loop from the abdomen, and after having sectioned it longitudinally, it was seen that it formed an enormous sac containing many kilograms of fecal material which was greenish brown, soft and did not contain scybala or foreign bodies. The intestinal walls were indurated and thick. Ulcerations were found on the mucosa. One of these ulcers was deep, almost annular and had perpendicular edges. The linear perforation already described was found at its base.

Microscopic examination, at low magnification, showed that the ulcer was funnel-shaped; the loss of substance occurred only in the mucosa and the musculature of the mucosa. The base of the ulcer was formed by the submucosa; the edges were perpendicular and were formed by the glandular layer of the mucosa and the musculature of the mucosa. One of the edges of the glandular layer was separated from the muscular layer which was destroyed, and at this level there was a free space separating this layer from the muscular layer. The other layers of the intestine were normal in appearance. Under higher magnification, it was found that the anatomic elements composing the glandular of the intestine in the vicinity of the edges of the loss of substance stained poorly; the nuclei of the glandular epithelial cells, as well as their protoplasm and the connective tissue of the wall of these glands had undergone coagulation necrosis. A short distance from the edges of the ulcer it was found that the anatomic elements preserved their normal structure. The base of the loss of substance was formed of loose connective tissue containing several round cells in its meshes; although the inflammatory process was relatively slight at this level, it was found, however, that this part of the submucosa contained many more embryonal cells than at other points of this tunic distant from the loss of substance. There was no appreciable ulceration of the vessels or the other layers of the intestine. In this case, the ulceration was chiefly due to necrosis of the superficial layers of the mucosa accompanied by a moderate inflammatory process in the subadjacent part of the mucosa.

CASE 25 (Gamgee,⁴⁸ 1898).—*Perforating Ulcer of the Sigmoid Flexure of the Colon.*

A man, aged 28, had ulcerative colitis in August, 1897. He suddenly had an acute pain in the inferior region of the abdomen on November 1. His temperature ranged between 100 and 101 F. for several days. A circumscribed tumor gradually developed in the left iliac fossa. The tumor was incised and about 3 drachms (11.09 cc.) of pus were obtained from a localized intraperitoneal abscess. Twelve days after operation, gas and the contents of an enema escaped through the wound. The fistula closed and the patient recovered.

48. Gamgee: Perforating Ulcer of the Sigmoid, Brit. M. J. 1:950, 1898.

hospital. At autopsy, a stercoral ulcer was found on the posterior wall of the cecum. There was a small perforation at the center. The appendix was normal but the cecum and colon were distended by feces. The distention was apparently due to atony of the intestines, because there was no obstruction along the course of the intestine.

CASE 23 (Guinard,⁴⁶ 1896).—*Perforating Ulcer of the Hepatic Flexure of the Colon.*

A man, aged 27, while in good health, suddenly was seized with violent abdominal pain. Laparotomy was performed thirty-six hours later. There was diffuse peritonitis. The appendix was simply congested, but was excised; its cavity was free. The patient died thirteen days after operation. At autopsy, there was a purulent area containing gas at the junction of the ascending and transverse colons. The omentum was thickened and black. There was generalized peritonitis at the hepatic flexure and a perforation the size of a 5 franc piece was found. The intestinal mucosa was greatly congested. No other ulcers were found in the digestive tract. The perforation of the colon was the primary cause of the symptoms.

CASE 24 (Morel and Rispaïl,⁴⁷ 1896).—*Ulcer of the Pelvic Colon; Perforation.*

The patient was a man, aged 67, who entered the hospital on April 26, 1896. His hereditary history was negative. He had never been seriously ill; however, since infancy, he frequently had dull pains in the abdomen, undoubtedly due to chronic constipation; his stools had never been regular and at times he had profuse evacuations of solid material. At the time of the first examination, constipation had lasted for one month. During this time, the patient had no desire to go to the stool. His appetite was preserved. Food did not produce any discomfort or sensation of weight; he had no fever and his facies were not altered.

Examination showed that the abdomen was large and tense. A tumor of cylindrical shape could easily be seen under the skin. It began in the cecal region, ascended obliquely and became lost in the left hypochondrium. Palpation showed that this swelling was hard, resistant and of uniform consistency throughout its whole extent. Percussion showed marked loss of resonance. The left side of the abdomen seemed to be effaced in contrast to the distention of the right side. On palpation, it seemed that the sigmoid and the descending colon were empty, and over these regions percussion gave the usual abdominal resonance.

Rectal examination did not show any tumor or stricture. The fingers seemed to penetrate into a sort of excavation, as if the rectal ampulla was dilated in all directions. It was completely empty and did not contain any fecal matter. On account of these different symptoms, a diagnosis was made of intestinal occlusion. Although the distended loop extended obliquely upward and to the left, and did not follow the course of the ascending and transverse colons, it was believed that the cause of the obstruction was at the splenic flexure. The nature of the obstacle could not be determined. Cancer was eliminated. The patient was placed on a milk diet and a purgative enema was given on the 22d. Castor oil was given on the 23d and repeated on the 24th; three stools. On the 25th, he had a spontaneous stool. There was pain at the level of the umbilicus, which soon radiated. He did not vomit. Death occurred suddenly on the 26th. The patient had refused any operation. At autopsy, the abdomen was greatly distended

46. Guinard: *Perforating Ulcer of the Hepatic Flexure*, Thesis Paris, June, 1896, no. 324.

47. Morel and Rispaïl: *Ulcer of the Sigmoid; Perforation*, Soc. de méd. et Toulouse, 1896.

several capillaries, although the lumen was perfectly outlined by the elastic membrane and the middle tunic. The presence of cicatricial tissue containing vessels in the interior of an artery can only be interpreted as representing an old thrombosis of this vessel.

CASE 27 (Tedenat,⁴⁹ 1902).—*Enormous Retrocecal Abscess; Multiple, Large Perforations at the Origin of the Colon; Secondary Suture; Cure.*

A man, aged 40, who had had good health up to the age of 26 years, while living in Brazil for four years, had had syphilis, malaria and beriberi; he drank alcohol to excess. He returned to France in 1889. He had chronic constipation with abdominal pains, frequent cough and was only in fair general condition. The present disease began on April 29, 1901, with sudden pains in the entire right side of the abdomen, radiating toward the thorax and groin, without vomiting, and without complete constipation. He remained in bed for twenty days with thirst and fever. His abdomen was slightly distended and was painful and tender on the slightest pressure.

The patient entered the hospital on May 21. He was pale and thin. His temperature was 40.2 C. (104.3 F.), and his pulse rate was 104 and small. There was sharp pain in the entire right half of the distended abdomen. The skin over the right iliac fossa was red. The cecum was distended and gave a dull tympanitic sound. Cough was paroxysmal and there was induration of the right apex.

Operation was performed on May 22. Roux's incision for appendicitis was made. The abdominal wall was indurated and bled freely. As soon as the peritoneum was opened, about 500 cc. of thick fetid pus mixed with gas and fecal matter escaped. The cecum was greatly dilated and was reddish-violet. There were grayish, false membranes on its antero-external surface, which was adherent to the parietal peritoneum. The appendix was of almost normal appearance and was found underneath the false membranes. On passing the finger behind the cecum, a large glassful of pus escaped. There were two rounded perforations, 12 and 15 mm. in diameter on the posterior surface of the colon a little above its origin. These perforations were about 3 cm. apart. At 4 cm. above the highest perforation, there were three other rounded perforations in a row, from 7 to 8 mm. in diameter. Two large rubber drains were placed behind the cecum and the entire perforated portion was surrounded with iodoform gauze and a large cotton dressing was applied. The patient passed a good night and on the next morning was much better; the temperature was practically normal; the pulse rate 69, and weak. On June 26, the patient's general condition was good. The fecal fistula still discharged. It was decided to close the fistula.

An operation was performed under chloroform. An incision 26 cm. long was made parallel to the first incision at one finger's breadth from the parietal fistula. The cecum was reached and the colon was separated from the abdominal wall. The intestine was almost normal. There was practically no change in the perforations on the posterior surface of the colon. Each of the perforations was closed with a purse-string suture, and the suture line was covered with peritoneum. A large rubber and gauze drain was inserted to keep the cecum and colon away from the incision. Dressings were made with compresses moistened with salt solution. In the evening, his temperature was practically normal; his pulse rate 98, and strong.

The patient left the hospital on July 26 with a granulating wound about 6 cm. long and from 1 to 2 cm. wide. The fistula closed. The intestine was not distended. There was no pain. The patient had a good appetite; his bowel move-

49. Tedenat, quoted by Quenu and Duval.

CASE 26 (Quenu and Duval,⁴ 1902).—*Simple Hemorrhagic Ulcer of the Rectal Ampulla.*

A woman, aged 50, entered the hospital for profuse rectal hemorrhages. The hereditary history was negative. She had three children, two of whom died of diarrhea and convulsions; the living child was 16½ years of age. There had also been two miscarriages. She had been treated for metritis after the first miscarriage, and had been sent to mineral springs. She had not had any other illnesses. The digestive tract functioned normally; digestion was good; she did not have diarrhea or constipation. The stools were normal and did not contain any mucus or membranes. She used alcohol somewhat to excess. The first rectal hemorrhage occurred in November, 1899. It appeared without any definite cause and was profuse. She had syncope, and her pulse became weak. A subcutaneous injection of salt solution became necessary. The second hemorrhage occurred in May, 1900; it was arrested by rest in bed and ice. She became weak. In July, 1900, there was a third hemorrhage accompanied by syncope, which was controlled by ice and rest in bed. The fourth hemorrhage occurred in July, 1901; ice and rest in bed were instituted as before. The fifth hemorrhage occurred on May 25, 1902. This was perhaps the most severe hemorrhage, and rapidly caused syncope. Two injections of aqueous extract of ergot and an injection of salt solution were given. On the following day, the patient did not have hemorrhage. The urine did not contain sugar or albumin.

She entered the hospital on June 22. Rectal examination showed only some anal varicose veins. With the speculum 8 cm. above the anocutaneous line at the junction of the posterior wall with the right lateral wall, the following was found: (1) a superficial ulceration with a pink base, 5 or 6 cm. long, from which the hemorrhage occurred; (2) a cicatricial band situated just to the side of the ulcer which bled easily. The ulcer was cauterized with the thermocautery on June 22, and the hemorrhage ceased. Tampons were placed in the rectum. Menstruation commenced on the afternoon of June 23, and during the night there was a severe rectal hemorrhage which required salt solution. The uterine hemorrhage soon ceased. Tampons were placed in the rectum. The ulcer was on the road to cicatrization on June 27, and on July 12 healing was complete and the patient left the hospital.

Microscopic examination revealed an ulcer of the rectal ampulla with arterial thrombosis. Serial sections were made following the axis of the extirpated ulcer. On each side of the sections it was found that the rectal mucosa had an absolutely normal cylindrical epithelium. On the base of ulcer, the epithelium and the mucosa were lacking. In their place there was a depression 1 mm. deep and 1.5 mm. wide. The base of this depression was formed by a fibrous zone rich in migratory cells (especially phagocytes) and covered with many red cells. It also contained some smooth muscle fibers which seemed to belong to the muscularis of the intestine. This fibrous zone rested on a dense, sclerous, cicatricial tissue which contained few cells and was intensely stained by fibrous tissue stains. This tissue not only formed the deep portions of the ulceration, but it extended on each side below the mucosa which rested directly on it without the interposition of a muscularis mucosa or any of the other layers of the intestine. The mucosa was thinner than normal and its interstitial tissue contained many leukocytes. The cicatricial sclerotic tissue contained a large number of capillaries. In addition, it surrounded a certain number of small veins and arterioles. The largest of these arterioles presented a remarkable disposition. It was found that in all sections the lumen was completely obliterated by a cicatricial fibrous tissue containing

ments were regular and his general condition good. Tuberculous granulations were not seen either around the perforations or on the peritoneum. There were no lesions resembling cecocolic tuberculosis of the hypertrophic form. Hence, tuberculosis may be eliminated as a cause of these rounded perforations with perpendicular edges. Can the lesions be attributed to syphilis? The syphilis had been well treated.

CASE 28 (Idem).—*Retrocecal Abscess in the Iliac Fossa and in the Fatty Tissue Around the Femoral Vessels in the Middle Part of the Thigh; Perforation of the Posterior Wall of the Cecum; Appendix Little or not Diseased; Death Due to Chronic Septicæmia.*

A man, aged 52, of good health, had had typhoid at the age of 18 years. On Aug. 10, 1891, after eight days of complete constipation, his abdomen became painful and he began to vomit. His condition was serious for four days and was attributed to intestinal obstruction. An enema produced a profuse evacuation. The same painful symptoms recurred on September 8. The maximum pain was in the right iliac fossa with radiation to the thigh. He did not vomit. There was an abundant discharge of gas through the anus. The stools became normal at the end of a week and the abdomen returned to its normal size, but the pain persisted in the iliac fossa and right thigh. He had continuous fever. A physician was called on September 20, and found a deep swelling in the iliac fossa extending to the middle part of the antero-internal surface of the thigh. The swelling increased progressively, remaining deep in the abdomen and becoming more superficial at the internal surface of the thigh. The patient entered the hospital on Oct. 12, 1891, thirty-four days after the beginning of this second attack. Although he continued to take milk and bouillon without vomiting, he was pale, thin, feeble and had hectic fever. There was a deep induration in the right iliac fossa. It extended to the median line without any marked redness of the skin and continued downward to the middle part of the thigh, elevating the vessels and thrusting them inward. The skin was red and adherent over the swelling in the thigh and showed fluctuation. There was an enormous edema of the entire leg. The intestine was moderately distended, but the abdomen was only slightly painful on pressure, except in the iliac fossa.

On October 13, an oblique incision 8 cm. long was made a little outside of the resonant protrusion formed by the cecum. Several adhesions were broken at the infero-external part of the thickened cecum and about 1 liter of fetid pus escaped. There was a perforation about 2 cm. in diameter on the external part of the posterior surface of the cecum. The purulent cavity was prolonged downward toward the true pelvis. A second incision was made 2 cm. below the crural arch. It was 6 cm. long and was parallel to and outside the femoral vessels. A counter opening was made behind the middle part of the tendon of the fascia lata. The crural focus communicated with the iliac focus through the crural canal. The cecum was adherent to the anterior abdominal wall. The purulent cavity was subperitoneal. The appendix was searched for in vain. Four drains were inserted. There was great improvement of the general condition for about twelve days. The patient took 2 liters of milk, bouillon and wine.

On October 25, there was a profuse discharge containing fecal material. The pains increased and the fever rose. Two days later, an incision of 5 cm. within and parallel to the first was made in order to reach the internal surface of the cecum, for the purpose of searching for another abscess, resecting the iliac portion or making an anastomosis. Some thin adhesions were separated. The appendix was practically free and was of normal appearance. It was found behind the cecum. It was rapidly resected. The operation had to be discontinued

the size of a 5 franc piece was found. This perforation was almost round and was situated on the antero-external wall of the ascending colon and was parallel to the axis of the intestine. The mucosa was invaginated. The appendix was adherent, but did not show any perforation. The perforation was excised and sutured. The patient's general condition improved, but the local condition did not show any improvement. The third operation, a median laparotomy with a transverse incision, was performed on July 18. The ascending colon was freed of numerous adhesions. Resection of 10 cm. of intestine with terminoterminal anastomosis. She was cured on August 7.

CASE 31 (Lyle,¹ 1912).—*Simple Ulcer of the Colon; Perforation.*

A woman, aged 26, was admitted to St. Luke's Hospital in October, 1909, with the diagnosis of acute appendicitis, with abscess. The history and clinical symptoms on admission appeared to be those of an acute suppurative appendicitis engrafted on a chronic appendicitis. On admission, her temperature was subnormal and the pulse rate, 92. A blood count showed 25,000 white cells, with 86 per cent of polymorphonuclears.

An incision was made over the mass, and a large abscess containing fecal matter was evacuated. On the inner wall of the cavity, about 2 inches (5 cm.) above the cecum, there was a large, oval, indurated ulcer, in the center of which was a perforation, with necrotic edges. The edges were trimmed, a section removed for examination, and the perforation was closed. The appendix was outside of the cavity and apparently had nothing to do with the condition, but as it might have been the source of the infection, it was removed. A small rubber dam drain was inserted and the wound was closed. The patient made an uneventful convalescence, and left the hospital twenty-three days later. Microscopically, the appendix showed nothing abnormal, and the section from the ulcer showed it to be a simple ulcer of the colon.

On March 12, 1912, the patient returned to the hospital for the correction of a ventral hernia springing from the scar of the former operation. When this operation was performed by Dr. Gibson, the only evidences found of the former ulceration were a few fine adhesions on the colon. The picture presented by the original condition was so striking that one might have believed he was dealing with a gastric perforation. After the operation, a more detailed history was obtained, and it was then learned that the patient had long been a sufferer from indefinite gastric symptoms. She had made the rounds of the clinics, and her condition had been variously diagnosed as ulcer of the stomach, gallstones, floating kidney, chronic appendicitis and cancer.

CASE 32 (Eunike,⁵¹ 1918).—*Simple Ulcer of the Colon.*

Louis Sch., aged 53, was admitted to the hospital on Feb. 28, 1918. His past history showed that an operation for double inguinal hernia had been performed several years previously, the right side being operated on first. The condition had recurred. The patient had always had difficulty in having bowel movements. He was often very constipated. Of late, he complained of severe pain in his abdomen. Eleven days before admission to the hospital, he began to have severe attacks of pain. His bowel movements were irregular and thin. For the past three days, he had been vomiting.

Physical examination revealed a strong, well nourished man, with a full, strong and regular pulse beat. Marked tenderness was elicited in an area over the

51. Eunike, K. W.: Ulcer Simplex of the Colon, *Deutsche Ztschr. f. Chir.* 147:284, 1918.

débris was eliminated in seven or eight days, and a large intestinal fistula became established. The general condition of the patient improved rapidly, but the fistula still discharged abundantly.

On March 16, operation was performed for the cure of the artificial anus, under an anesthesia of a mixture of alcohol, chloroform and ether. A flap of skin 6 cm. long and 3 cm. wide was excised. There was a slight prolapse of the intestinal mucosa. It was separated with difficulty, inversed and sutured with a Lembert suture. The tissues were friable. The principal perforation was rounded and 2 cm. in diameter. Above this perforation there were two others, slightly smaller, separated by bridges of intestinal wall 1 to 2 cm. wide. These perforations were located at the origin of the colon. A resection of the ileocecal segment with partial resection of the colon was decided on. The lower end of the parietal incision was enlarged downward and inward and the upper end directly upward. The cecum was separated, drawn outside the wound with the terminal portion of the ileum and the first 10 cm. of the ascending colon. Forceps protected by rubber were applied on the colon 8 cm. from the ileocecal valve and on the ileum at the same distance from its opening into the cecum. A wide, lateral anastomosis was made between the ileum and colon over a distance of 5 cm. The terminal sections of both ends of the intestine were sutured. The edges of the wide and thick mesentery of the large intestine were sutured. All of these sutures were made rapidly with Lembert sutures of fine silk. The intestinal wall was sutured in three layers with the exception of a distance of 2 cm. through which a drain was passed to the line of intestinal sutures. A compressive dressing was applied.

On May 4, the patient was considered cured. He had a good appetite and digestion was easy. The stools were regular. The general condition was excellent and he had gained weight. Examination of the tissue showed that the cecum was congested; the wall slightly thickened, but there were no traces of ulceration of the mucosa. The ileocecal valve was soft. The three perforations were spread out over an extent of 6 cm., beginning at the origin of the colon. They were rounded and had a punched out appearance. The edges were slightly thickened and indurated. There were no traces of cancer or tuberculosis. The appendix was 8 cm. long, straight, regular in size and normal; its walls were soft. There were no adhesions, ulcerations or scars. The excised skin was thickened by a simple chronic inflammation. There was infiltration of leukocytes with bands of sclerotic connective tissue.

CASE 30 (Zickler,⁵⁰ 1910).—*Perforation of the Ascending Colon.*

The patient was a woman, aged 25, without any previous history. She had had her first child a month previously. The confinement was normal. On May 25, while in the toilet, she had a sudden violent pain in the lower part of the abdomen which soon decreased, but later reappeared with greater intensity and was accompanied by vomiting. She entered the hospital thirty-six hours after the onset of symptoms. On admission, she had symptoms of peritonitis and diagnosis was made of appendicitis.

Laparotomy was performed on May 27. On account of the serious condition of the patient, nothing could be done except to remove the feces in the abdominal cavity and drain. Her condition improved a week after the operation. A second operation was performed on June 2. The pus pocket was cleaned, and a perforation

50. Zickler: Perforation of the Ascending Colon, *Beitr. z. klin. Chir.* 67:184, 1910.

believed that he had an intestinal obstruction in all probability due to cancer of the larger intestine. On admission to the hospital, he was in bad general condition; his complexion was earthy, his features drawn, and slight jaundice of the conjunctiva was noted. The pulse rate was about 100; the temperature, 38.5 C. (101.3 F.). Since his admission, the patient vomited several basins full of greenish fluid. His abdomen was distended, tense and was extremely painful throughout. The slightest pressure produced contraction of the muscles. There were no peristaltic contractions of the intestine. The arrest of feces and gas had been progressive and seemed to be total. It was thought that he had an occlusion due to cancer, but considering the condition of the patient, his temperature, the sharp pains on palpation and finally the appearance of the vomitus, it was suspected that this neoplasm was accompanied by inflammatory phenomena.

A median laparotomy was performed. When the abdomen was opened, it was seen that the intestinal loops were dilated, red and adherent to each other by means of fibrinous adhesions. The entire abdomen was carefully explored, and it was found that the right edge of the omentum was thickened and indurated and extended toward the right iliac fossa. It was adherent to the anterior wall of the ascending colon at its origin. It was carefully raised and was easily detached allowing the upper surface of the large intestine to be seen. Just above a line passing through the upper border of the intestine at its opening in the cecum, there was a regular circular perforation the size of a 50 centime piece. Its edges were sharp, hard and was located in the middle of a small indurated zone. This perforation was immediately closed with a tampon, and an incision was immediately made in the right iliac fossa, through which the portion of the large intestine on which the ulcer was situated was exteriorized. The exteriorization was maintained by fixing the intestine to the abdominal wall by means of several catgut sutures. This was done to gain time as the patient was already weak, and it was believed that the cecoiliac fistula thus established would have a good effect on both the peritonitis and on the intestinal obstruction. The intestinal loops were cleansed with ether through the median incision, and the operative incision was closed. A large drain was placed in Douglas' culdesac. Unfortunately, the patient died during the night following operation. The large intestine was removed at the autopsy. It presented no other lesion except the perforation which was situated at the origin of the colon on its anterior surface. The mucosa of the ascending colon and cecum seemed to be normal. With the exception of the induration which surrounded the ulcer, which was of slight extent, no other alteration of the intestinal wall could be found. The specimen was sent to a laboratory for examination, but unfortunately was lost so that no histologic examination could be made. Macroscopic examination showed that this perforation was distinctly different from those seen in ordinary ulcerations of the intestine and no lesion was found which could explain its production.

CASE 35 (Idem).—Perforation of the Cecum.

A youth, aged 20, was admitted to the hospital on Jan. 20, 1903, for appendicitis. He was operated on for an abscess of appendicular origin on February 25. A right lateral incision was made along the external border of the right rectus muscle. As soon as the peritoneum was seen, it was evident that pus would be found; in fact, on opening the abdomen, a creamy greenish pus with fecal odor escaped. After having sponged this pus, it was found that the intestinal loops were adherent to each other. The hand was passed along the abdominal wall until the posterior wall of the cecum was reached. At this time bubbles of gas

abdomen, which was tympanitic. Both herniae recurred. On the right side, there was a small recurrence and a light, pale small operative scar. The left hernia was about the size of a man's fist and was irreducible and tense. A diagnosis of strangulated left hernia was made.

An operation was performed on the left hernia under local anesthesia. The whole sigmoid flexure was tied down with adhesions and the wall was markedly hypertrophied. The incision was enlarged, and gas anesthesia administered. On enlarging the incision, there was a fibrous exudate, the form and color of which resembled that coming from a perforated ulcer of the stomach. Under deep general anesthesia, the hernia was repaired and an incision was made from the xyphoid to the navel. Again appeared the fibrous exudate. The stomach was found to be normal, but on the hepatic flexure a perforation could be seen. The wall of the bowel was much infiltrated. The perforation was sewed with considerable difficulty. The ligatures were cutting through. Tamponade and drainage was instituted. The patient made a good immediate convalescence, but died on the fifth day after the operation. Autopsy showed general peritonitis. The sutures on the hepatic flexure held. In the close proximity of the perforation, there were three or four small ulcers. The rest of the colon did not show any signs of a pathologic process. The whole large intestine was hypertrophied.

CASE 33 (Soupault,⁸ 1920).—*Perforation of a Simple Ulcer of the Colon.*

A woman, aged 22, was admitted to the hospital suffering from abdominal disturbances of acute onset. The diagnosis of appendicitis had been made, with the surmise that in the course of an acute attack with remission, perforation had occurred some hours before the patient's entrance.

Operation was performed, the Roux incision of 10 cm. being used. Incision of the peritoneum promptly revealed on the anterior aspect of the presenting coil, a perforation the size of a small pea, from which fecal matter escaped. The perforation was immediately closed with forceps, and the intestinal coil (cecum and ascending colon) was gently wiped off with a moist compress. The perforation was found to be situated on the antero-internal border of the ascending colon, 10 cm. above the cecum. The rounded perforation measured from 4 to 5 mm. in diameter. The borders were slightly thickened and ecchymotic. The surroundings were slightly swollen and edematous, but not indurated. The intestinal wall was flaccid and hyperemic. The peritoneum had lost its normal sheen and presented a few false membranes. The appendix, lying in the focus of peritonitis, was not seriously affected, but was resected. The perforated ulcer was rapidly sutured with linen thread purse-string suture; a second seroserosus layer was closed by a U suture. The coils were irrigated with ether and two drains were placed in Douglas' space and in the iliac fossa, respectively. The wall was closed in two layers. The operative procedure took thirty minutes. The patient made a good recovery.

CASE 34 (Bazy,⁵² 1920).—*Perforation at the Origin of the Ascending Colon*

A man, aged 65, was brought to the hospital with symptoms of progressive intestinal occlusion. He had been having violent pains in the abdomen for eight days. He experienced severe colic which was generalized over the entire abdomen. He vomited. For two or three days, there had been the complete arrest of feces and gas. Interrogation of the patient showed that he had had intestinal disorders for a long time, and on several occasions he had presented painful crises accompanied by vomiting. He had chronic constipation. For these reasons, and considering the age of the patient, the physician who sent him to the hospital

was situated 3 cm. above the insertion of the appendix. The appendix was normal as well as the rest of the large intestine. The perforation had allowed fecal matter to pass into the peritoneum, and especially beans of which the patient had eaten a large quantity twenty-four hours before the beginning of symptoms. The edges of the ulcer were indurated and it had the appearance of an old lesion. The patient was a heavy eater and had chronic constipation. For three months he had been having discomfort in the right iliac fossa.

CASE 38 (Lardennois,⁵⁵ 1920).—*Spontaneous Perforation of the Cecum.*

A man, aged 52, gave a past history which showed that he had had lead colic during the previous year, which had appeared while he was working on storage batteries. In addition, he presented evident signs of lead poisoning. Later, he suffered from digestive disorders and anorexia, difficult digestion and constipation. On September 9, while walking to work, he suddenly had a severe pain in the right iliac fossa and had to be taken home. A short time later, nausea and vomiting occurred. According to the patient's story, the right iliac fossa was extremely painful and the vomiting persisted. There was no evacuation of feces or gas. His condition improved slightly after several days, and on September 12 he took a purgative. He had several stools following this purgative, but the symptoms rapidly became worse and he was brought to the hospital during the night of September 16 in a dying condition. On admission, it was found that he had peritonitis. A median laparotomy was performed. Cloudy fluid was found in the entire abdomen. There were abundant false membranes. There was a circular perforation with sharp edges about 5 mm. in diameter on the cecum. It was at the most protruding portion of the antero-internal wall and appeared to be larger at the level of the mucosa than at the serosa. The appendix seemed to be normal. The cecal opening was rapidly closed. The appendix was removed for examination. Inspection of the abdomen did not show any other lesion. There was no other ulcer, nor was cancer perceptible on careful examination. The adhesions were liberated, and the intestines were washed with ether. Drainage was instituted. The patient died during the course of the following night.

A later examination showed nothing more than was found during the operation. The appendix did not present any lesion other than those of superficial congestion due to its presence in an area of peritonitis. Histologic examination was not made.

CASE 39 (Schoemaker⁵⁶).—In 1906, the author treated a man who had been sick for five days. The patient had always been in good health previous to this time. On Sept. 12, 1906, he suddenly had a sharp pain in the abdomen which was followed by vomiting. At first the pain extended over the entire abdomen, but little by little it became localized in the lower part. The pain diminished in intensity while his general condition became worse. He was sent to the hospital on September 17. On admission, his appearance was bad. He had a characteristic peritoneal facies. Rectal examination showed that Douglas' pouch was distended and painful. The diagnosis was acute appendicitis (low appendix which had perforated and had given rise to an abscess in the true pelvis).

An incision was made in the median line from the symphysis almost to the umbilicus. On opening the peritoneum, a large amount of fetid pus escaped. The cavity was emptied and dried with gauze tampons. The loops of small intestine were adherent to each other. The appendix was found. It was red like the intes-

55. Lardennois: Bull. et mém. Soc. de chir. de Paris 46:447, 1920.

56. Schoemaker, quoted by Soupault.

were seen to arise, and at the same time the characteristic noise of intestinal perforations was heard. The appendix was twisted on itself and adherent, but there were no special lesions. On the other hand, a certain distance away from it on the anterior surface of the cecum was found a circular perforation which easily admitted the tip of the index finger. This perforation was easily closed by a double line of silk sutures. The appendix was removed. A drain was left in the abdominal cavity. The abdominal wall was closed in three layers. The patient left the hospital, cured, on April 7, 1903.

CASE 36 (Gregoire,⁵³ 1920).—*Perforation of an Ulcer of the Sigmoid.*

A man, aged 55, of robust constitution but with chronic constipation, had passed stools on several occasions which contained blood. He attributed this to hemorrhoids. On June 1, 1919, while walking, he had pains in the lower part of the abdomen and was obliged to go home. He thought that constipation was the cause of the pain, and he took an enema. When he went to the toilet, he suddenly had a violent pain with vomiting. There was violent colic. He went to the hospital seven hours later. On admission, he was in great pain but his general condition did not seem to be bad; the temperature was 37.8 C. (100 F.); the pulse rate, 104. His abdomen was greatly distended and painful throughout. There was an absolute arrest of feces and even of gas. On account of the sudden onset of these peritoneal symptoms, it was thought that he had acute appendicitis with general peritonitis. Operation was performed seven and a half hours after the beginning of the symptoms.

A right iliac laparotomy was performed. On opening the abdomen, a rather large quantity of grayish fluid mixed with fragments of feces was discharged. However, nothing was found at the ileocecal angle or at the level of the appendix. A small amount of fecal material was found in the true pelvis. The iliac incision was then lengthened downward and inward, and the epigastric artery was ligated. The true pelvis could then be easily explored. It was literally filled with an enormous quantity of hard and pasty feces. After cleaning out the pelvis, a perforation the size of a 50 centime piece was found on the anterior surface of the sigmoid. The edges were slightly indurated for a short distance, and beyond the induration the mucosa of the colon was apparently normal. The edges of the perforation were resected, and the loss of substance was sutured in two layers. Although the peritoneum and the intestine did not appear to be inflamed, extensive drainage was inserted on account of the presence of such a large amount of feces in the abdomen.

During the following days, the patient seemed to support the operation well, there was no vomiting, his general condition was good, and he passed gas spontaneously. However, there was abundant suppuration from the abdomen. It was later learned that on June 16, this man again had abdominal pain with profuse vomiting which became fecaloid, and he died. It was believed that these symptoms were due to probable occlusion. Autopsy was not performed.

CASE 37 (Sieur,⁵⁴ 1920).—*Perforation of the Cecum.*

The patient was a man about 30 years of age. When the author saw him he had an acute abdominal attack which was so serious that it was thought advisable to send him to the hospital at once. The surgeon at the hospital did not believe that he would be able to operate and the patient died three days later. At autopsy, a perforation of the cecum was found. It was the size of a 50 centime piece.

53. Gregoire: Bull. et mém. Soc. de chir. de Paris 46:420, 1920.

54. Sieur: Bull. et mém. Soc. de chir. de Paris 46:421, 1920.

middle of the tumor proved to be an area about the size of a 2 mark piece covered with a fibrin deposit. On bimanual palpation, from the lumen of the intestine through an invagination in the wall of the cecum, this area was found to be a crater-shaped, rather long oval, sharp-edged ulcer, the inner and outer finger tips being separated from each other by a thin layer. The appendix did not show any pathologic change.

An appendectomy was performed. The pathologic part of the wall of the cecum was invaginated and buried in two stages by serosa sutures so that normal serous surfaces came together. Suture of the wall of the abdomen was done in two stages, without drainage. On April 16, the wound healed by first intention. Bowel movements were obtained only after enema. The patient's condition was good. In the histologic specimen of the appendix (serial sections), no pathologic changes were noted, particularly no tuberculosis. On April 25, the patient was up. Enemas were still necessary for bowel movements. Repeated examination of the stools for tuberculosis bacillus were negative. On May 11, a stool was passed after a purgative without any symptoms. The patient weighed 129 pounds (58.5 Kg.). She was discharged from the hospital cured.

CASE 41 (Ecot and Richard,²⁵ 1922).—*Perforation of a Simple Ulcer of the Ascending Colon.*

This recent observation on a perforation of a simple ulcer of the ascending colon, seen by the authors in the Service of Professor Pieree Duval, is of particular interest from the clinical point of view (syndrome of occlusion) as well as the anatomic point of view, the only one here considered. The specimen was removed in the course of the operation and showed a rounded, punched-out perforation of from 6 to 8 mm., with thickened margins, situated on the antero-external aspect of the ascending colon, 10 cm. above the ileal opening. The perforation permitted the escape of fluid material and gas; the patient at the time was suffering from perforation peritonitis. Excision of the ulcer, suture of the colonic wound and drainage were followed by recovery. Direct polymorphonuclear infiltration around the glands was visible at one extremity of the specimen. Embryonic infiltration was noted, especially abundant at the level of the muscular mucosa. Diffuse sclerosis, separating the fibers of the muscular mucosa layer, and perivascular sclerosis were also present, but no endarteritis. The capillaries were dilated and there was diffuse hemorrhagic infiltration. The serosa was slightly thickened. Accordingly, the condition was evidently long-standing mild sclerosis of the colon, apparently simple, as specific lesions of syphilis, tuberculosis or cancer, were not demonstrable at any point. The course of the disease became complicated in the following days by intestinal obstruction. An artificial left iliac anus was made.

CASE 42 (Dickinson,² 1922).—*Perforating Ulcers of the Cecum.*

A man, operated on, April 3, 1895, had had acute right inguinal pain and tenderness. There was no tumor. The rectal temperature was 101 F. The condition was diagnosed as appendicitis. A right rectus incision was made. The appendix was normal. The cecum was enormously distended, with three points of impending perforation 6 cm. in diameter. The peritoneum was reduplicated over these. Necropsy, five days later, revealed that the points of suturing held, but there were six new perforations in the cecum. These ulcerations were punctate, round, sharp margins, not necrotic.

CASE 43 (Idem).—A man, aged 22, operated on, Dec. 4, 1916, had suffered for a number of years with gassy dyspepsia, sour brash and delayed digestion, with relief on vomiting and never any pain. There was some discomfort in the

tine, but it was no more inflamed than the intestine and there was no perforation. A small round hole was found in the sigmoid from about 3 to 5 mm. in diameter, and about 12 cm. above Douglas' culdesac. The edges were infiltrated, and its appearance was that of a perforated ulcer of the stomach. The edges were excised, and a small wound in the intestine was closed. Drainage was established and the abdomen was partially closed.

The patient went into collapse on September 18. His pulse was scarcely palpable, and in spite of stimulants, he died in the evening.

Autopsy revealed normal thoracic organs. The stomach and the small and large intestines were opened. No inflammation of the mucosa or ulcer was found. The mucosa near the small intestinal wound in the colon was normal. Microscopic examination of the edge of the ulcer showed an infiltration of white cells. There was no evidence of tuberculosis.

CASE 40 (Levy,⁵⁷ 1921).—*Simple Ulcer of the Colon.*

E. F., a servant girl, entered the hospital on April 9, 1920. There was no history of tuberculosis in the family. She always had enjoyed good health until three years before, when she began having "stomach pain" lasting from one to two hours, which was so slight that she paid little attention to it. In September, 1919, she was treated for the first time in a hospital for pain that came on suddenly in the right side of the abdomen. She was discharged in ten days. She was admitted to the hospital again in January, 1920, for the same symptoms. Since that time she has frequently suffered from constipation and had to take purgatives. Three days before her present illness, she complained of dull pain over her whole abdomen which decreased a little after the passage of gas and a single stool, but the day before admission increased and became localized in the right side of the abdomen and from that time on was continuous. She did not suffer from vomiting. A hard stool was passed spontaneously in the night with severe pain. After that, the pain decreased considerably, but began again after about three hours.

Examination on admission, on April 9, 1920, revealed a large, strong girl in an excellent condition of nutrition. The left half of the abdomen was soft, without rigidity and without pain, and was compressible. On the right, a little inward from McBurney's point a rather long, oval, moderately hard tumor the size of a small hen's egg could be felt; it was movable and sensitive, particularly in the central part. There was no abdominal rigidity on the left and a trace on the right. Gynecologic examination revealed the uterus retroflexed, and no swelling of the adnexa.

The symptoms seemed to suggest appendicitis, though the symptoms on palpation left serious doubt of the diagnosis. The movable tumor inward from McBurney's point did not fit into the picture of appendicitis, in which the tumor, if there is any, is generally fixed firmly in the hollow of the sacrum. But operation seemed to be indicated.

Operation (Prof. Alsberg) was performed under general anesthesia. When the abdominal cavity was opened, turbid-serous fluid gushed out. A hard tumor could be felt on the wall opposite the ileocecal valve when the cecum was pulled out; it was about 3 by 6 cm. in size, long, hard, smooth and a little indented in the middle. Its red color was distinctly different from the velvet-red of peritonitis and showed dilatation and branching of the vessels. The inflammation of the

57. Levy, Alfred: Simple Ulcer of the Colon, *Deutsche Zeitschr. f. Chir.* 105: 356, 1921.

CASE 47 (Chalier and Mallet-Guy,⁵⁹ 1923).—*Simple Ulcer of the Ascending Colon.*

A man, aged 50, was admitted to the hospital on Oct. 3, 1921, with evidence of active pulmonary tuberculosis. Nothing else abnormal was found, and there was nothing to indicate any disorder of the digestive tract. This condition persisted without any marked change up to Jan. 23, 1922, with a temperature ranging between 99.6 and 101.1 F. On this date, diarrhea occurred without any previous colic and there was an intestinal hemorrhage. There were four stools of red blood without clots amounting to about 1 liter. At the same time his temperature went down to 98.9 F. and the patient became pale and anemic. He complained of vertigo and marked asthenia. The hemorrhage was relieved by rest, diet, applications of ice to the abdomen, by the administration of small, very hot enemas and the administration of calcium chloride and epinephrine. Several days later, when all danger seemed to be over, a careful and complete examination of the patient was made to determine the cause and location of the hemorrhage.

The respiratory symptoms were not changed. Rectal examination was negative. No abdominal tumor could be palpated, but the spleen was increased in size and extended about 2 inches beyond the costal border. In addition, there was dulness in the flanks which moved with a change in position and showed the presence of a slight degree of ascites. The intestinal hemorrhage was not repeated, and one and a half months before death he began to complain of pains in the umbilical region. He had a permanent burning sensation which was better after taking food. Three hours later there would be a marked increase of the pain. At this time the pains would be sharp, radiating to the left shoulder and persisting for two or three hours. They never terminated in vomiting, but were relieved by evacuation of the bowels. Diarrhea generally occurred. There were five or six stools daily, sometimes preceded by slight colic. His appetite was fair. Palpation was painful in the right iliac fossa. It was even more painful in the epigastric region just below the xyphoid and no tumor could be felt. His general condition became worse and it was not believed advisable to cause him to undergo the fatigue of a x-ray examination. Being confined to bed with his diet restricted, he rapidly became cachectic and he died on April 8, 1922.

At autopsy, the lungs showed evidence of tuberculosis. The right suprarenal capsule, to a large extent, showed caseation. The left suprarenal was normal. On the ascending colon about 5 cm. above the ileocecal valve, there was found on the antero-external surface an ulceration arranged transversely, perpendicular to the axis of the colon. This ulceration was of linear form about 1 cm. long and from 1 to 2 mm. wide. The edges of the ulcer were slightly elevated and were dark. The base of the ulcer appeared to reach the subserosa. There was no peritoneal reaction at this level. On examining the serosa, a small vessel could be seen by transparency. It was in a direction perpendicular to the axis, and a part of its course was exactly in relation to the base of the ulcer. This vessel was obliterated at a point in its course which corresponded to the center of the ulcer; it was undoubtedly this vessel which gave rise to the intestinal hemorrhage. The entire mucosa of the ascending colon was pink, while this coloration was absent in the rest of the intestine. The mucosa of the large intestine presented many folds without any appreciable lesions. No ulcer or other lesion was found on the small intestine, duodenum or stomach.

59. Chalier, J., and Mallet-Guy: Simple Ulcer of the Ascending Colon. Arch. d. mal. de l'appar. digest. 13:521 (June) 1923.

appendicular region. The condition was diagnosed as chronic appendicitis or cholecystitis. The gallbladder was opened, disclosing dark bile, thickened with mucus, but no calculi. Drainage was instituted. The remainder of the abdomen was apparently normal on palpation and exploration, with the exception of the appendicular region. A second opening was made. The appendix was clubbed, fibrous, and excised through the tip of the cecum. On manipulation of the cecum to explore adhesions, a ligature in the cecal incision pulled off, with discharge of a substance resembling a dysenteric stool. The stoma was religated with linen thread. Necropsy, on the fourth day, revealed the ligature on the appendix stump in place. There was a ragged perforation of the cecum the size of a 5 cent piece opposite the ileocecal junction.

CASE 44 (Idem).—A man, aged 50, operated on, July 21, 1921, a clerk of good habits, experienced abdominal trouble three weeks before, starting with severe pain at the umbilicus, and green, watery vomitus. This recurred with intermissions. During the second week of the present illness, the pain shifted to the right lower quadrant. Vomiting continued, the vomitus becoming brown. The patient had been given considerable bismuth. Roentgenograms were taken. There had been no action of the bowels in ten days. On admission to the hospital, the patient presented marked pyorrhea, coated tongue and reddened throat. Pain, rigidity and tenderness were noted at the cecal region, particularly on deep pressure. The heart sounds were distinctly heard at the pubes. As some type of appendicitis was suspected, an incision was made through the right rectus sheath. When the peritoneal cavity was opened, a puff of gas was heard. The peritoneum and viscera were markedly injected, and purplish red. The appendix was normal. The cecum was agglutinated to the lateral wall. When it was lifted up, liquid feces exuded from several small openings in the ulcerated areas, about opposite the ileocecal junction. These points of ulceration were about 6 cm. in diameter. In view of previous experiences, the cecum was stitched to the abdominal peritoneum and incised freely. Bismuth feces were removed. Convalescence was protracted, and during it the patient developed exfoliated stomatitis, associated with which was complete anorexia and an intolerance by the stomach even for water, except in small quantities.

CASE 45 (Bowen,⁵⁸ 1922).—*Perforation of the Large Bowel.*

A woman of middle age with a negative gastric history was taken suddenly with severe abdominal pain, nausea and vomiting. Eight hours later, the abdominal wall was rigid and the signs indicated a perforation. Operation revealed fecal material in the abdomen, and a perforation of the sigmoid. The walls of the colon were described as rotten, and they only tore on attempts to suture. The woman died, but autopsy was not permitted. The author was unable to get a clear idea of the abdominal condition, but thinks the perforation probably resulted from thrombosis. Evidence in favor of a stercoral ulcer or foreign body was scanty.

CASE 46 (Idem).—A woman, aged 27, who had been suffering from gastric ulcer, developed severe pain all over the abdomen, with a definite right sided rigidity, and maximum tenderness just above and internal to the anterior superior spine. Operation revealed an acute catarrhal appendicitis, with a perforation in the cecum, near the ileocecal valve. There was no free fluid in the abdomen, the perforation having been closed by some valve action. As no constipation had been present, a stercoral ulcer can be ruled out.

58. Bowen, W. H.: Five Cases of Perforation of the Large Bowel, *Guy's Hosp. Rep.* 72:441 (Oct.) 1922.

ulcer was caused by a fecolith. The perforation orifice was found to contain a hard fecal mass. The symptoms observed during life, at the time of perforation, in the form of profuse hemorrhage from the anus and sudden onset of pain, were explained by the (microscopically) distended and congested vessels, which extended almost to the intestinal lumen. In spite of her advanced age, the patient had been in good condition up to a few months before her admission to the hospital on account of general weakness. As she suffered from chronic constipation, cascara was regularly administered. Her condition some months later was entirely satisfactory, when she was suddenly attacked by severe abdominal pains. The abdomen was painful on palpation, with some muscular defense. On three occasions, the patient passed a few small scybala with about 75 and 100 cc., respectively, of fluid, unchanged blood, without mucus. The results of the rectal examination were negative. At night, her hands became cold and the heart sounds became weaker; the pulse rate was 120 and weak. In the course of the next day, the temperature rose, the condition became aggravated, the pulse rate increased to 160, was weak and small, and at the end of the second day after the onset of the symptoms of perforation, the patient died. The autopsy explained all symptoms, indicating that the microscopically greatly congested vessels, reaching nearly to the intestinal lumen, were responsible for the profuse hemorrhages from the anus at the time of the perforation, with simultaneous onset of severe pains.

CASE 50 (Boss,²¹ 1927).—*Perforating Ulcer of the Large Intestine.*

A man, aged 38, entered hospital on Aug. 8, 1921. Eleven years before he had had gastro-intestinal catarrh while in Arabia which lasted eleven days; ten years before he had had malaria in India. There were no further intestinal disorders. On August 7, the afternoon previous to his admission, while in perfect health, he had had sudden, violent, convulsive pain in the umbilical region and vomiting. On August 8, the day of admission, he passed a black stool. Vomiting and pain persisted in spite of the administration of narcotics. Peritonitis was suspected, and he was sent to the surgical ward of the hospital. On admission, physical examination showed him to be a robust man, in fair condition of nutrition, healthy appearance of skin and face. The blood picture revealed 11,200 leukocytes with 90 per cent polymorphonuclears. The temperature was 102 F.; pulse rate, 110, regular and full. The results of the physical examination were negative except that in the abdomen, the scaphoid was indrawn; there was intensive resistance, and the greatest pressure pain in the region between the navel and the symphysis. The urine was normal. A diagnosis of peritonitis was made, and operation was immediately performed.

A median laparotomy was performed. The small intestines were reddened. There was some pus deep in the pelvis. It was more abundant in the median line than in the region of the appendix. The appendix was free and was found not to be responsible for the peritonitis. The intestines in the pelvis were covered with fibrin. In the lower portion of the sigmoid, there was a perforated ulcer the size of a bean from which feces were discharged. The tissue in the vicinity of the ulcer was not infiltrated but reddened. The ulcer was closed by five longitudinal catgut sutures and two rows of catgut sutures. To relieve the strain on the sutures, a broad colostomy was made in the descending colon, three handbreadths above the suture line.

Two days after operation, there was a large stool from the fecal fistula. The patient made an uneventful convalescence and was discharged as well on December 15. Four weeks after operation sigmoidoscopy revealed a normal condition of the mucosa for 22 cm. The ulcer had disappeared.

Histologic examination revealed a simple ulcer of the colon without any tuberculous or neoplastic formation. The edges of the ulcer were raised. The ulcer had extended through the muscularis mucosa and had deeply penetrated the muscular layer. This progression was accompanied by a marked lymphocytic reaction. The vessels of the subserosa were obliterated. The right suprarenal was cascated, but there were some traces of glandular tissue. Giant cells were found. The section included a sympathetic ganglion, which was normal.

CASE 48 (Mintz,⁵⁷ 1923).—*Simple Ulcer of the Colon.*

A girl, aged 18, took sick with vomiting and abdominal pains, evacuation of fifteen nematodes took place five days after castor oil had been given. Within the next eleven days, intermittent attacks of colic and constipation occurred. On the sixteenth day, the attending physician established evidence of a mobile tumor in the ileocecal region and prescribed oleum chenopodii, whereupon another ascaris was evacuated. On the seventeenth day, during examination in my department, an extremely mobile tumor was found below the umbilicus. The diagnosis of chronic invagination was confirmed by the x-ray examination. Seven hours after ingestion of the contrast meal, the lower ileum and also part of the ascending colon were filled, and the invagination of the ileum loop could be directly seen on the plate. Stools that resembled the fecal matter of sheep were passed on the same day. On the evening prior to operation (twentieth day of the disease), the colicky pains, which had been constant and slight, became more severe. The tumor became enlarged to a cylinder which disappears obliquely upward to the left underneath the costal arch. Later on, vomiting set in. Immediate surgical intervention was advised. The ileum, cecum and ascending colon were invaginated into the transverse colon. Disinvagination of the edematous intestinal parts was performed without difficulty. In the cecum, a hard indentation of the wall, opposite the orifice of the ileum was noticeable. This was the size of a 1 mark piece. The serosa over it was thickened and flaming red—in short, the picture was presented that one sees on the serosa over peptic ulcers. Typical ileocecal resection was performed. The patient had an uneventful postoperative course.

The cecal wall as a whole was unchanged. The indentation appeared to have been due to the inflexibility of the diseased place in contrast to the distended, healthy adjacent parts. On the mucous membrane, there was a sharply defined ulcerated surface of the size of a 1 mark piece which corresponded to the indentation. This surface was of brownish red and contrasted markedly from the completely healthy appearing adjacent mucous membrane. A similar ulcer the size of a pea was situated 1 cm. away from it, at the same level.

Microscopic examination revealed the serosa considerably thickened, with newly formed dilated vessels. The larger ulcer showed a sharp demarcation from the surrounding area, loss of mucous membrane, small celled infiltration and scattered necrotic foci, which are also found in the muscularis. On the little ulcer, similar conditions were found which did not penetrate so deeply. Thrombosing endarteritis could not be demonstrated.

CASE 49 (Broere,⁶⁰ 1923).—*Decubitus Ulcer of the Colon.*

This contribution comes from the Pathologico-Anatomical Laboratory of the Wilhelmina Institute in Amsterdam, and concerns the autopsy observations in the case of an old woman 80 years of age. An ulcer was found at the transition of the rectum into the sigmoid flexure of the colon. Rupture of a so-called decubitus

60. Broere, W. J.: Decubitus Ulcer of the Colon, Nederl. Tijdschr. v. Geneesk. 67:2274, 1923.

"STREAM LINE" PHENOMENA IN THE PORTAL VEIN AND THE SELECTIVE DISTRIBUTION OF PORTAL BLOOD IN THE LIVER *

GLOVER H. COPHER, M.D.

AND

BRUCE M. DICK, M.B., F.R.C.S. (Edin.)
ST. LOUIS

There have been a few experimental and clinical studies that have suggested the possible occurrence of a selective distribution of portal blood in the liver and the presence of independent currents of blood in the portal vein. Final proof of the presence of these currents has not been established, and the selective distribution of portal blood in the liver has been held in doubt. The possible existence of segregated streams of blood in the portal vein and their subsequent distribution to definite parts of the liver is of interest and should be of considerable practical significance in the study of the physiology and pathology of the liver. The evidence in favor of the existence of these phenomena has not generally been known or seemingly accepted.

In 1901, Sérégé¹ injected india ink into the splenic vein of the dog and found particles only in the left lobe of the liver; when the ink was injected into a tributary of the large mesenteric vein, particles were found only in the right lobe. These experimental observations were confirmed by Glenard.² Bauer³ and several other workers repeated the experiments, but they were unable to distinguish any difference in the distribution of the india ink, and therefore denied the existence of a dual portal current. In 1907, Loeb⁴ found that the iodine content of the right lobe of the liver of rabbits was constantly greater than that of the left one hour after subcutaneous injection of potassium iodide. This observation was confirmed by Wells⁵ and Hedenburg.

* From the Department of Surgery, Washington University School of Medicine, and Barnes Hospital, St. Louis.

1. Sérégé, H.: Contribution à l'étude de la circulation du sang porte dans le foie et des localisations lobaires hépatiques, *J. de méd. de Bordeaux* **31**:271, 291 and 312, 1901.

2. Glenard, F.: Note sur les localisations lobaires hépatiques, *Bull. et mém. Soc. méd. de hôp. de Paris* **18**:386, 1901.

3. Bauer, A., and Brissant, E.: L'indépendance des lobes du foie est hypothèse, *J. de l'anat. et de la physiol.* **45**:1, 1909.

4. Loeb, O.: Die Jodverteilung nach Einfuhr verschiedener Jodverbindungen. *Arch. f. exper. Path. u. Pharmacol.* **56**:321, 1907.

5. Wells, H. G., and Hedenburg, O. F.: Studies in the Biochemistry and Chemiotherapy of Tuberculosis: The Permeability of Tubercles for Iodin Compounds and Proteins, *J. Infect. Dis.* **11**:349, 1912.

Röntgen-ray examination of the intestine after a barium meal and a barium enema showed that in passage from the descending portion of the large intestine into the sigmoid flexure, a constriction occurred, lasting several hours, at a point which corresponded to the location of the sutured ulcer. The following history was obtained from the patient some time after his operation: Six months before the perforation, the patient had had an accident while carrying a heavy load. He had slipped and fallen, injuring his back. From that time on he had had considerable abdominal pain when lifting heavy weights.

Cases 51, 52 and 53 are my cases 1, 2 and 3 which have been reported earlier in this paper.

and be maintained in the portal vein, we made a careful study of the portal system and its tributaries and also of the mode of termination of the portal vein in the liver.

THE ANATOMY OF THE PORTAL VEIN IN THE DOG

Mode of Termination of the Portal Vein at the Hilum of the Liver.

—At the hilum of the liver, the portal vein divides into two main branches; the division takes place at an angle of about 170 degrees. The right branch of the portal vein is smaller and has a much shorter course than the left branch.

The right branch of the portal vein is distributed entirely to the two lobes of the liver which lie most laterally. After a short course outside the liver, the vessel divides into two or four branches, and one, or a pair of these, passes into each of the two right outer lobes.

The left branch of the portal vein traverses the hilum of the liver for a distance of about 5 cm.; in its course it gives off three branches which come off at right angles to it and pass directly to the three intermediate lobes of the liver; some of these branches may be paired. The main vessel ends by dividing in a radiate manner into five branches; each of the two large left lobes receives two branches, while the fifth branch passes into the small lobule of liver which is situated immediately to the left of the gallbladder; this lobule also receives a branch from the main left trunk (figs. 1 and 2).

It will be observed that strict *anatomic* bilaterality of the portal vein does not obtain in the dog's liver as it does in that of the human subject. In the dog, the left branch of the portal vein supplies two thirds of the whole organ; the right branch of the portal vein delivers blood only to the two outer right lobes of the liver.

Intrahepatic Course of the Portal Vein.—The intrahepatic course of the portal vein was studied in specimens in which iodized oil (40 per cent) had been injected into one of the tributaries of the portal vein in a living dog. Roentgenograms of the excised livers were taken, and an exact outlining of the venous channels was obtained (fig. 2).

It was observed that the main vein of each lobe splits up in an arborescent fashion, and that there is no anastomosis between the larger branches. The larger branches of the portal vein and their smaller ramifications are clearly displayed in figure 2. When livers from human beings had been injected with iodized oil 40 per cent a similar distribution of the portal vessels was demonstrated; furthermore, the strictly sectorlike distribution of the large portal branches suggest that the human liver may be regarded as a multilobar organ resembling closely the dog's seven lobed liver.

In 1914, Bartlett,⁶ Corper and Long studied the problem. Olive oil emulsified in blood serum was injected into different parts of the portal system of the dog. After counting the number of fat emboli in microscopic sections of different parts of the liver, they concluded that a dual portal current exists in the dog's portal vein; and that blood from the stomach, spleen, duodenum, first portion of the jejunum and rectum flowed mainly to the left lobe of the liver, while blood from the lower portion of the jejunum, the ileum and the first portion of the large intestine flowed mainly to the right lobe.

More recently, McIndoe⁷ and Counseller made anatomic studies of the liver in man by means of the celloidin-corrosion method; these studies indicate an anatomic division of the liver into two separate units. These workers have demonstrated that the area of distribution of the right and left branches of the portal vein in the human liver is sharply divided along a line from the fossa for the gallbladder to the entrance of the hepatic veins into the inferior vena cava, and that the only communication between the two vessels is through intercellular sinusoids. The same line of demarcation separates the field of supply of the branches of the right and left hepatic artery and also the branches of the two hepatic ducts. The line of lobar separation, as determined by the celloidin method, corresponds to the recognized embryologic boundary between the right and left lobes of the liver.

In the present investigation, we made a study of the blood currents in the portal vein itself, and observed the subsequent distribution of the blood in the lobes of the liver. Dyes were injected into different radicles of the portal vein of the dog, and their ultimate localization in the liver was observed. The advantages of this method are that the injected material can immediately be visualized in the part of the liver to which it has been conveyed, and that the dye-stained blood can be seen in the portal vein when the vessel is submitted to powerful transillumination. The method overcomes the objections to the use of particulate matter for intravenous injections.

At the outset of this experimental study, emulsified iodized oils were introduced into various parts of the portal circulation, and roentgenograms of the liver were obtained. An unequal distribution of the iodized oil was often noted, but the site in the liver in which the oil localized itself was inconstant.

As we believed anatomic considerations would be of importance in determining the way in which a system of stream-lines might arise

6. Bartlett, Corper and Long: The Independence of the Lobes of the Liver, *Am. J. Physiol.* **35**:36, 1914.

7. McIndoe, A. H., and Counseller, V. S.: Bilaterality of the Liver, *Arch. Surg.* **15**:589 (Oct.) 1927.

portal vein; it joins the mesenteric vein at an angle of about 45 degrees. About 2 cm. from its termination, it receives a branch from the posterior part of the stomach and lesser curvature.

Large Mesenteric Vein⁸: The large mesenteric vein is larger than the splenic vein; it drains blood from the lower part of the duodenum and the whole of the small intestine. Near its termination it has a linear course, and the portal vein appears to be a direct continuation of it.

The small mesenteric vein⁸ enters the large mesenteric vein at an angle of about 5 degrees, less than 1 cm. below the point of union

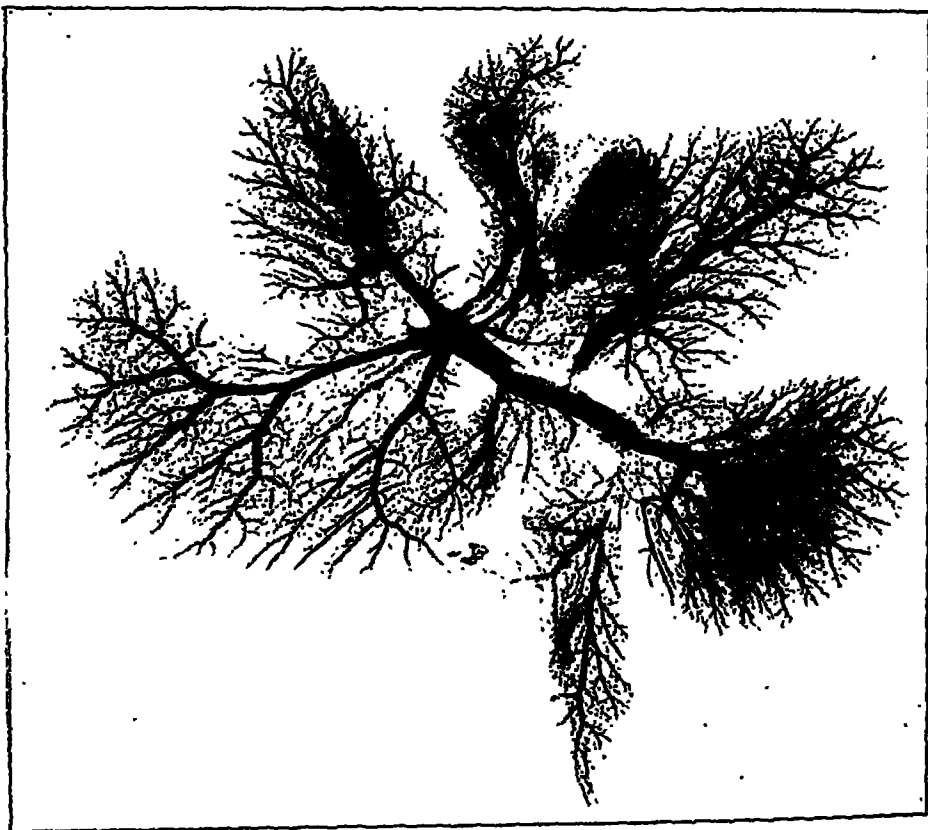


Fig. 2.—Dog's liver after intraportal injection of iodized oil. Note the arborescent character of the large portal veins and the absence of large intralobar anastomoses.

of the splenic and large mesenteric trunks. The small mesenteric vein drains blood from the whole of the colon; it has two main branches. The right branch comes from the cecum and the first part of the colon; the larger left branch collects blood from the distal part of the colon and rectum. The two branches unite into a short common stem that

8. In works on anatomy of the dog the mesenteric veins are called large and small. The large vein corresponds to the superior vein of the human subject; the small vein corresponds to the inferior mesenteric vein.

The Anatomy of the Portal Vein and of Its Tributaries.—In the dog, the average length of the portal vein is 8 cm. It begins dorsal to the neck of the pancreas by the union of the splenic and large mesenteric veins. The vessel runs in a cephalad direction, dorsal to the superior part of the duodenum, between the two layers of the lesser omentum to the right end of the porta of the liver, where it divides into a right and a left branch.

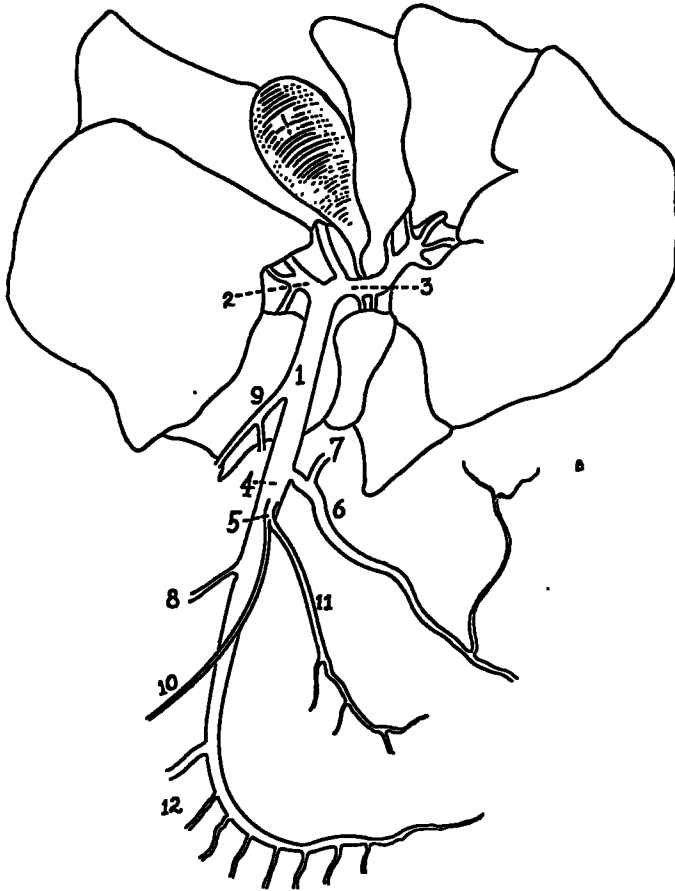


Fig. 1.—Diagram of the portal system of the dog showing the main tributaries and the mode of termination of the vessels at the hilum of the liver. 1 indicates the portal vein; 2 and 3, the right and the left branch of the portal vein, respectively; 4, the main mesenteric vein; 5, the small mesenteric vein; 6, the splenic vein; 7, the gastric branch of the splenic vein; 8, the lower pancreaticoduodenal vein; 9, the upper pancreaticoduodenal vein; 10 and 11, the right and the left branches of the small mesenteric vein and 12, the enteric branches of the large mesenteric vein.

Tributaries: The chief tributaries are the splenic, the large mesenteric and the upper pancreaticoduodenal vein.

Splenic Vein: The splenic vein runs to the right from the hilum of the spleen and ends by joining the large mesenteric vein to form the

lobe of the liver constantly received a portion of the dye. The remainder of the right side of the liver retained its normal chestnut color, and the dye did not register itself in any part of it.

Stomach: The injection was made into a small vein on the lesser curvature. The whole of the left half of the liver was uniformly stained by the dye. The line of separation between the right and left lobes was sharply demarcated and thrown into striking contrast by the unilateral staining of the liver. No trace of dye was recognized in the right side (fig. 3).

Pancreas and Upper Part of Duodenum: An injection was made into the superior pancreaticoduodenal vein. The dye was constantly carried to the right side of the liver; the two lobes on the extreme right of the liver were deeply stained. A small amount was deposited in the right border of that lobe which adjoins the two more lateral lobes (fig. 4).

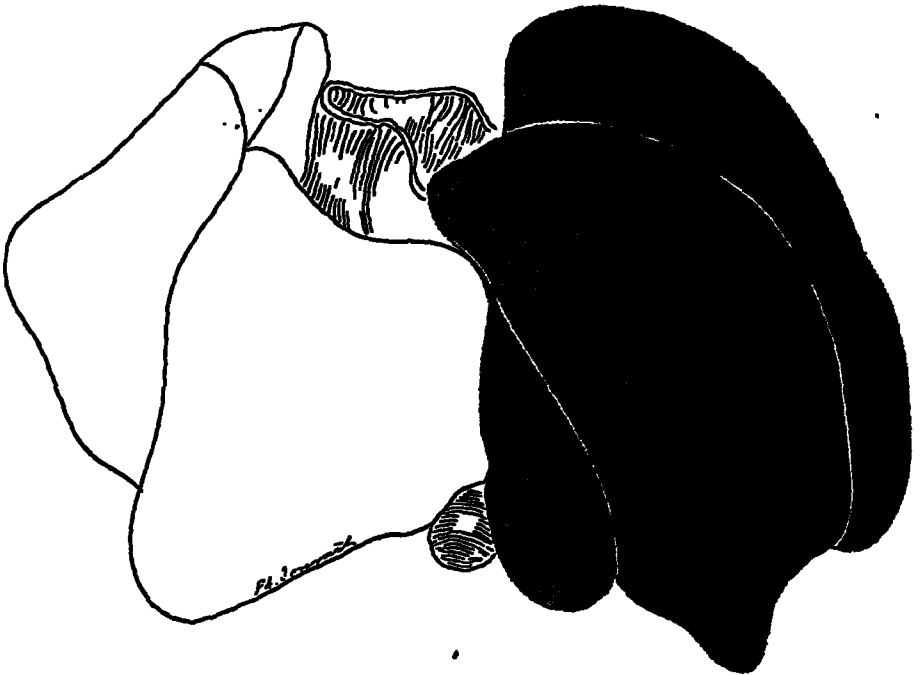


Fig. 3.—Dog's liver drawn from a specimen to illustrate the distribution of trypan blue after the injection into a gastric branch of the splenic vein. The black area denotes the part of the liver that was stained by the dye.

An injection was made also into the inferior pancreaticoduodenal vein. The dye was carried mainly to the right half of the liver, although a certain amount reached the left side. The lobe which lay immediately to the right of the gallbladder always showed deeper staining than any other part of the liver.

Jejunum: Dye was injected into a mesenteric vein at the highest part of the jejunum. The bulk of the dye registered itself in the two extreme right lobes of the liver. Scattered spots of coloration were seen occasionally in the left half of the liver but never more than a few (fig. 5).

Cecum and Appendix: A small vein at the root of the meso-appendix was selected for injection. The dye was transported to all parts of the liver. The large outer left lobe of the liver generally showed a greater deposition of dye than other parts, and was stained more deeply than the rest of the liver. In some dogs, the right half of the liver showed a greater amount of dye than the left.

enters the left side of the large mesenteric vein a little toward its ventral aspect. In some dogs, the right and left branches of the small mesenteric vein do not unite to form a common vessel, but enter the large mesenteric vein separately at the same level. In such instances, the branch from the left portion of the colon enters on the left side of the large mesenteric vein, and the right terminates about the center of the ventral aspect of the main mesenteric trunk.

Pancreaticoduodenal Veins: There are two of these vessels. The upper pancreaticoduodenal vein drains the head of the pancreas and the first part of the duodenum and also receives a small tributary from the pyloric area. The vein ends by joining the portal vein on its right side, about 2 cm. below the hilum of the liver. The lower pancreaticoduodenal vein derives blood from part of the head of the pancreas and the distal part of the duodenum; it ends by joining the right side of the large mesenteric vein about 5 cm. from the termination of this vessel.

EXPERIMENTAL STUDY OF THE DISTRIBUTION OF THE PORTAL BLOOD CURRENT IN THE LIVER

Method.—Trypan blue, dissolved in blood serum, was employed as the coloring agent for the study of the portal blood current. One gram of trypan blue crystals was dissolved in 15 cc. of blood serum; 3 cc. of this solution was the amount generally given at each intravenous injection of the portal radicles; the quantity was varied slightly according to the size of the dogs employed. The advantages of the dye are its lightness and solubility, and the parts of the liver to which it is conveyed by the blood stream are immediately colored. The staining of the liver persists for some time, and formaldehyde preservation of the specimens does not obliterate the coloring.

The dogs were anesthetized with ether, the abdomen opened, and the various portal tributaries injected with trypan blue solution; the animals were killed with ether soon after the injections, and the liver was removed for examination. Injections were, as a rule, made into the smallest veins that could be easily entered by a hypodermic needle; care was taken not to disturb the normal position of the viscera when the injections were being carried out. About thirty seconds was the average time taken to complete an intravenous injection, and only gentle pressure was employed. In some instances, the position of the animal on the operating table was altered in order to study the effect of posture. The experiments were repeated many times for each part of the portal vein that was under investigation. In all, about 100 experiments were performed.

Sites of Injection and Results.—In the following descriptions, the liver is regarded as being divided into right and left halves by a line passing from the fossa for the gallbladder to the entrance of the hepatic veins into the inferior vena cava. It was noted that in the canine liver this division does not correspond to the anatomic distribution of the two main branches of the portal vein.

Injection of Splenic Vein: A venule at the lower end of the hilum was selected for injection. Almost the whole of the left lobe of the liver was colored by the dye. It was observed that a limited area of the upper part of the extreme right

The Disappearance of the Dye from the Liver.—In some instances, the behavior of the dye in the liver was observed before the animals were killed. It was noticed that when the dye had restricted itself to a particular portion of the liver there was only a slight tendency for diffusion to occur to a part beyond the initial site of localization. After from five to ten minutes, the dye commenced to disappear from that part of the liver in which it had first deposited itself. The liver as a whole assumed a slightly darker color throughout, but only to the same degree as the other organs of the body that, for a time, became tinted light blue when the dye reached the systemic circulation.

The Effect of Large Injections of Dye.—When the trypan blue was injected in a large quantity the liver was colored throughout, but the staining was not equal in all parts; for example, if a large volume of dye was injected into the splenic vein the whole liver became blue, but the staining was always more pronounced in the left side.



Fig. 6.—Distribution of dye after injection of a vein in the mesentery of the lower part of the colon.

VISUALIZATION OF THE CURRENTS WITHIN THE PORTAL VEIN

Method.—The peritoneum was denuded from the surface of the portal vein and its larger tributaries near their termination. The experiments were carried out in a darkened room. A Cameron curved abdominal light that transilluminated the interior of the vessels was placed immediately behind the portal vein. The moving blood current was evident at once, when the light was placed in situ. Small dogs were used in these experiments so that effective transillumination of the portal vein could be obtained more readily. Trypan blue dissolved in blood serum was introduced into different branches of the portal system, and the transilluminated portal vein was kept under observation while the injections were being made. The injections were made slowly and with great gentleness.

A striking demonstration of sharply defined intraportal currents was afforded by this method, and the extreme rapidity of blood flow in the portal vein was made evident.

Sites of Injection and Results.—*Splenic Vein.* The injection was made near the hilum of the spleen. The dye-stained blood was seen to enter the left side of the portal vein obliquely. The dark stream kept strictly toward the left side of the

Descending Colon and Rectum: The large vein in the mesentery of the left part of the colon was selected for injection. The dye was distributed throughout the liver. A greater amount of dye was evident in the left side, more especially in the large lobe on the extreme left side of the liver (fig. 6).

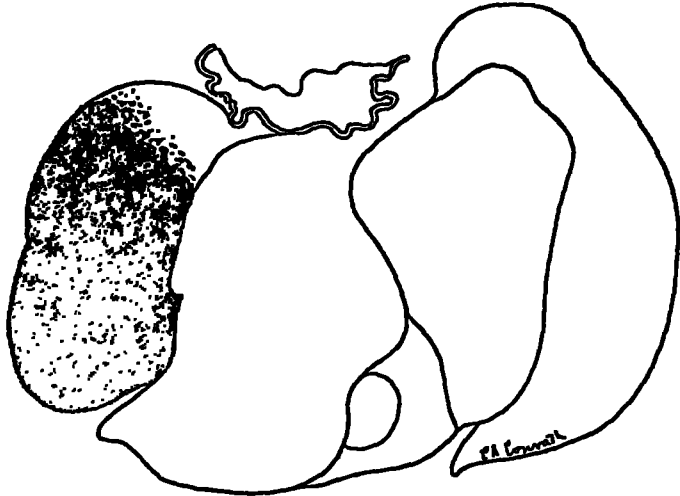


Fig. 4.—Distribution of dye after the injection of trypan blue into the upper pancreaticoduodenal vein of the dog. The darkly shaded area indicates the part of the liver to which the dye was carried.

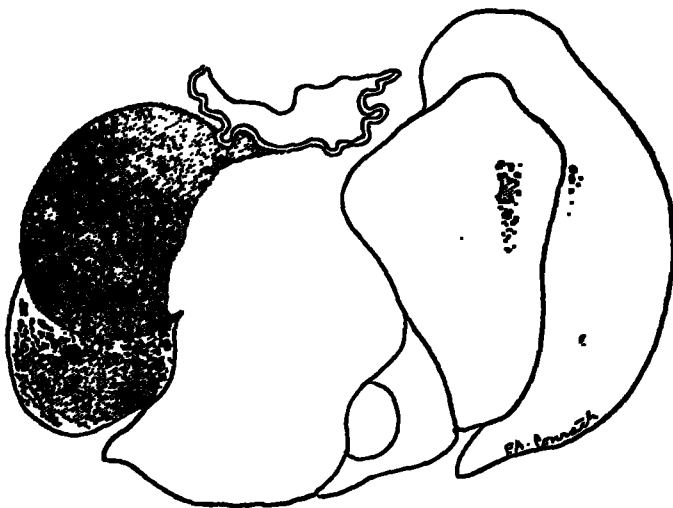


Fig. 5.—Distribution of dye after the injection of a mesenteric vein of the upper part of the jejunum of the dog.

Large Mesenteric Vein: The dye was injected at a point just distal to the entrance of the small mesenteric vein. The dye was deposited in the two lobes at the extreme right of the liver; a little was carried to the lobes of the left side.

The Effect of Posture.—Alteration of the position of the animal on the operating table, such as turning the trunk to one side or supporting the animal in the quadruped position while an injection was made, did not alter the character of the experimental observations.

It may be inferred from these facts that possibly blood that has been conveyed from the periphery of the portal system to a particular section of the liver is utilized in that specific area without contact with blood from other parts of the portal tree. It is of interest to note that, according to our experimental observations, the blood which is carried to the left lobe of the liver is drained principally from those abdominal organs that are not strictly engaged with the digestion or absorption of food, namely, the spleen, the stomach and the greater part of the colon; whereas, the blood collected from those parts of the alimentary tract where the products of digestion are absorbed is carried to the right side of the liver and, in the dog, often to a special and constant site in that lobe. For example, the blood from the upper pancreaticoduodenal veins is conveyed to the two lateral lobes of the right side of the liver.

In brief, it would seem from our evidence that there are areas in the liver which are especially supplied with blood from specific parts of the portal system, and that the blood from the different parts of the portal system does not become mixed in the liver nor, as we shall indicate, in the portal vein itself.

An explanation for the selective distribution of the portal blood in the liver is afforded by the visual demonstration of stream lines in the transilluminated portal vein after the injection of dyes. These currents serve to transport blood from the periphery of the portal system to the liver in such a manner that little or no intermingling of the individual blood streams occurs in the main portal channel. It would seem from our experiments that there are at least three main blood currents in the portal vein. These currents are, in our opinion, derived from three sources, namely, the splenic vein, the large mesenteric vein and its branches and the small mesenteric vein. In our observations, three sets of currents were initiated and maintained in the portal vein by these three large vessels.

Maintenance of individuality of different currents in the portal vein finds a counterpart in at least one other human circulatory system. In the fetal heart, blood from the superior and inferior vena cava does not mix freely in the right auricle. Likewise, the individual currents in the portal vein may be likened, in part, to the union of two rivers, for example, the Rhone and the River Avre, one clear and the other muddy, that retain their identity for a considerable distance after their union in a common stream-bed. This phenomenon of separate streams in a moving body of water is well known to hydraulic engineers and is usually discussed under the name of "stream lines." The anatomic disposition of the splenic, large mesenteric and small mesenteric veins would seem to be favorably adapted to the ejection of blood into the main portal channel in such a direction that the

portal vein and preserved a narrow, ribbon-like course throughout the portal vein up to the hilum of the liver. No mixing with the adjacent blood in the portal vein was observed, and a cleancut linear division between the narrow splenic and the broad mesenteric streams was seen throughout the length of the portal vein. The injection was continued for several minutes, and at no time was there any alteration in the character of the current.

Injection of Jejunal Vein: A vein in the mesentery of the upper part of the jejunum was selected for injection. The stream was narrow and was sharply demarcated. It maintained an undeviated course along the right wall, and no mixing with red blood was seen to occur as it traveled to the hilum of the liver.

Small Mesenteric Vein: The large vein in the mesentery of the descending colon was selected for injection. A thin linear current of blood was visualized in the center of the ventral aspect of the portal vein. The current preserved an absolutely undeviated course throughout the length of the portal vein, and diffusion into other parts of the vessels did not occur.

COMMENT

We have found by the injection of trypan blue into tributaries of the portal vein of dogs that, with few exceptions, the dye is transported in the portal blood stream to fairly constant and definite areas in the liver, and that the site varies according to the place at which the dye is introduced peripherally. In our experiments, we found that when trypan blue was injected into the veins of the stomach and spleen it was conveyed by the blood to the left half of the dog's liver almost entirely. Dye injected into the veins of the upper part of the duodenum, the head of the pancreas and the jejunum was carried to the right lateral lobes almost exclusively. When the veins of the colon were injected, the dye was distributed to all parts of the liver, but more particularly to the large lobe of the left side. In those instances, in which the two colonic veins did not unite in a common mesenteric trunk but had a separate termination in the large mesenteric vein, it was found that injection of the right vessel resulted in a more liberal distribution of the dye in the right side of the liver.

Trypan blue stains the parenchyma of the liver and the coloration remains for some time. Once the dye is carried to a particular region of the liver, the staining remains sharply circumscribed. The terminal character of the lobar divisions of the branches of the right and left portal vein and the absence of interlobar and intralobar venous anastomoses are responsible for the absence of visible diffusion to other parts of the liver. The temporary staining of the liver does not signify that the blood which conveyed the dye has itself remained confined in a demarcated area of the liver for so long a period, as the dye is almost immediately recognizable in the systemic circulation after intraportal injection; furthermore, the volume of flow of portal blood through the liver is rapid; in the dog, 60 cc. of blood per hundred grams of liver in a minute.

THE RÔLE OF THE CIRCULATION IN THE HEALING OF FRACTURES

A REVIEW

WILTON H. ROBINSON, M.D.

PITTSBURGH

Normal Blood Supply of Bone.

Effect of a Fracture on the Adjacent Arterial Circulation.

Effect of Cutting the Veins and Lymphatics at the Site of Fracture.

Incompressibility of Muscle Tissue and the Effect of This on the Circulation of Blood to a Fracture Area.

Relation of the New Bone Trabeculae to Blood Vessels.

The Laying Down of Lime Salts.

Development of Fibrous Tissue.

Summary.

Conclusions.

In 1863, Hamilton¹ estimated the incidence of nonunion of fractures to be one in 500 cases. Scudder and Hey-Groves,² in 1927, placed it, respectively, at from 2 to 3 and from 3 to 5 per cent. If it is true, but this is doubtful, that there is a larger percentage of delayed unions and nonunion of fractures today than formerly, it may easily be accounted for by the greater traumatisms sustained today and by the more exacting standards under which the surgeon works, but whether it is true or not, the fact still remains that a better conception of all the vital processes concerned in bone repair will result in diminished morbidity.

In this article are presented some salient facts relative to the circulation and its possible relation to the repair of a fracture.

The repair of a fracture is by a group of interrelated processes by no means well understood. These processes are: (1) the establishment of the circulation in preparation for the definite construction of bone; (2) dissolution, partial or complete, of the old bone and the laying down of lime salts to form new bone, which, architecturally, is not the same as the old, and (3) rearrangement of the new bone to carry the particular stress to which that section of bone is subjected.³ While these processes occur in the order given, they overlap so that two or even all may be going on at the same time. Throughout all processes of bone repair, the circulation is of primal importance, and by this is meant, not only the arterial circulation, but that of the veins and lymphatics, for without the elimination of the waste products, repair will be impossible.

1. Hamilton, F. H.: *A Practical Treatise on Fractures and Dislocations*. Philadelphia, Blanchard and Lea, 1863, p. 61.

2. Bancroft, F. W., and Scudder, C. L.: *The Treatment of Fractures*, ed. 10. Philadelphia, W. B. Saunders Company, 1926, p. 949.

3. Koch, John C.: *The Laws of Bone Architecture*, *Am. J. Anat.* 21:177 (March) 1917.

individual streams could remain separate. These anatomic advantages are probably further aided by the known differences in the rate of flow in the veins, their relative tonicity and differences in viscosity of the blood they contain.

SUMMARY AND CONCLUSIONS

1. The distribution of the portal blood in the liver of the dog was determined by the injection of a dye.

2. Blood from the spleen, the stomach and a greater part of the colon goes to the left lobe of the liver; whereas blood from the duodenum, the head of the pancreas and the upper part of the jejunum goes mainly to the right lobe of the liver.

3. A satisfactory method of visualizing experimentally the individual currents of blood in the portal vein is presented.

4. There are at least three distinct and separate currents in the portal vein.

5. The anatomy of the portal vein and the intrahepatic distribution of its blood in the dog were studied and the results have been presented.

EFFECT OF A FRACTURE ON THE ADJACENT ARTERIAL CIRCULATION

It may be accepted as axiomatic that repair of a fracture depends on the establishment of adequate channels of blood circulation to the injured area. Kolodny has shown by injected specimens⁸ that following a fracture there is increase in the diameter and in the tortuosity of all the arterial vessels in the section of the limb adjacent to the fracture.

Coincident with the occurrence of a fracture of a long bone there is damage to the normal blood supply. The longitudinal vessels are torn or cut by the shearing action of fragments, and the periosteal vessels are torn where the periosteum is separated from the cortex of the bone by avulsion. Bleeding immediately occurs from the injured vessels. In due time, a clot is formed about the fragments; lineal projections of this clot extend into the lumen of the arterial vessels until they reach the nearest patent collateral, and thus thrombi are formed in the vertical trabecular spaces of the bone for a varying distance below and above the actual line of fracture.

The clot in the longitudinal bone channels, i.e., the thrombi and that between the fragments, must be spoken of separately. The former no doubt will resolve by the same processes as will a thrombus of soft parts, where granulation tissue gradually replaces the clot and develops terminally into fibrous tissue with obliteration of the vessel, waste products being carried off by the leukocytes in the venous or lymphatic stream.⁹ With all the arterial longitudinal vessels crossing the site of the fracture blocked by thrombi and in progress of obliteration, any blood supply from them to the seat of fracture is impossible. The clot between the fragments, however, is gradually replaced by granulation tissue,¹⁰ which results in a close network of thin-walled vessels. These vessels become thicker by the growth of adventitial cells, some of the connective tissue and others of the plasma cell group; thus fibrous tissue develops progressively. Obviously, at this time there is little help in repair given by the arterial vessels of the cortex, which are plugged by thrombi. The granulation tissue starts from buds from functioning vessels. These may be from the medullary cavity, but they are mostly from the area surrounding the fracture,¹¹ where the greatest activity,

8. Kolodny, A.: The Periosteal Blood Supply and Healing of Fractures, *J. Bone & Joint Surg.* 5:698 (Oct.) 1923.

9. Keen, W. W., and DaCosta, J. C.: *Surgery, Its Principles and Practice*, Philadelphia, W. B. Saunders Company, 1920, vol. 1, p. 418; vol. 2, p. 104; vol. 5, p. 165.

10. Blaisdell and Cowan (footnote 6). Bancroft and Scudder (footnote 2, p. 927). Eising, E. H.: Remarks of the Physiology of Bone in Relation to Bone Diseases, *Am. J. Surg.* 3:368, 1927.

11. Bancroft and Scudder (footnote 2, p. 927).

NORMAL BLOOD SUPPLY OF BONE

The outer layers of the long bones are nourished by the periosteum; the inner layer, by the medulla. Blood vessels run longitudinally through the bone in a series of canals called the haversian canals, around which the bony lamellae are grouped. Another series of vessels passes from the periosteum into the interior of the bone through minute orifices. The medullary or nutrient arteries enter the bone through the periosteum and, traversing the cortex at a sharp angle, enter the medullary cavity, the length of the artery in the cortex being relatively short. The epiphysis is supplied from vessels which anastomose around the joints from three sets of vessels: the diaphyseal, the metaphyseal and the epiphyseal; thus epiphyseal vessels communicate with those in the metaphysis,⁴ and as the ramifications of the medullary or nutrient artery connect with the vessels in both the compact and the cancellous bone, anastomoses exist among all the arterial vessels in a bone. Johnson⁵ maintains that the metaphyseal arteries are second in importance to the nutrient arteries in nourishing the medulla; the inner half of the cortex receives its nutrition from the medulla, and the outer half of the cortex is nourished by the periosteal vessels.

The periosteal blood vessels subdivide rapidly before entering the cortical bone. As the blood vessels enter the haversian and Volkmann's canals, they are surrounded by delicate sheaths of areolar tissue; through continuity with the endosteal arcade, this areolar tissue is attached to the wall of the canal, and this gives support to the more or less centrally located vessels.⁶

The veins and lymphatics are probably no less important to the healing of fractures than are the arteries. The veins emerge from the bone in three places: (a) one or two large veins accompany the medullary (or nutrient) artery; (b) numerous large and small veins emerge at the articular extremities, and (c) many small veins pass out from the compact substance.⁷ Lymphatic vessels have been traced by Cruikshank into the substance of the bone, and Klein describes them as running in the haversian canals.⁷ A point that one should keep in mind is that when bone is divided, its vessels do not contract into the canals in which they are contained.⁷

4. Boyd, W. M.: *Surgical Anatomy*, Philadelphia, W. B. Saunders Company, 1925.

5. Johnson, R. W., Jr.: *A Physiological Study of the Blood Supply of the Diaphysis*, *J. Bone & Joint Surg.* 9:153 (Jan.) 1927.

6. Blaisdell, F. E., and Cowan, J. F.: *Healing of Simple Fractures*, *Arch. Surg.* 12:619 (March) 1926.

7. Gray, Henry; and Lewis, W. H.: *Anatomy of the Human Body*, Philadelphia, Lea & Febiger, ed. 21, 1924, p. 87.

Henderson and Brink¹⁴ demonstrated this in 1908 by carefully conducted physical experiments. While muscle changes its shape in contracting and expanding, it does not change its volume. Since muscle is a colloidal solution, albeit retained in its form by its sheath or its other fibrous interstitial structures, it will have the physical characteristics of a fluid. In the case of a fracture of a long bone, pressures are created against and in the muscle: (1) by displacement by hemorrhage, (2) by hemorrhage into its own interstitial structure from the trauma which caused the fracture and (3) by infiltration of inflammatory products around and into the muscle tissue. This increase in volume is apparent as swelling and is not in itself harmful or prejudicial to repair of a fracture; however, if such swelling is prevented, a series of maladjustments in pressures ensue which are deleterious not only to the circulation to the fracture, but to the muscle tissue itself. As an example of the latter, ischemic paralysis may be mentioned. In this article, only the effects of pressure on the circulation of the fracture are considered. It has been shown how pressure in and about muscles is created; this pressure may be resisted by heavy layers of fascia and by tightly applied splints, bandages, adhesive plaster or casts. If resistance to expansion (swelling) occurs, its effect will be to diminish or occlude the lumen of the arterial blood vessels and thus prevent an adequate supply of blood from reaching the interior of the callus. I believe that, regardless of the exact manner in which mineral salts are laid down, they are carried by the arterial system to the region in process of repair. If this belief is correct, interference with an adequate supply of blood must have a deleterious effect. It will be shown subsequently that granulation tissue is converted into fibrous tissue, which, by its inherent power of contraction, eliminates the very vessels by which it was formed. If, however, sufficient bone tissue has been laid down while the new vessels were still patent, they will make a more or less permanent connection with the general circulation and persist through the period of their need. Hence the great importance of an effort to prevent considerable hemorrhage and inflammatory reaction even during the early days of a fracture is evident, or if this should occur, the immediate provision for the additional expansion by a readjustment of any circumferential dressing whether it is a bandage, cast or adhesive plaster.

While a generalized pressure of surrounding tissues may occlude the arterial part of the circulation to a fracture, it has the opposite effect on the veins and incidently also on the lymphatics. These vessels are provided with valves which, not allowing a backward flow, cause the thin contained fluid (blood or lymph) under pressure to move in only one

14. Henderson, L. J., and Brink, F. N.: The Compressibilities of Gelatine and Solutions of Muscle, *Am. J. Physiol.* 21:248 (Feb.) 1908.

the most active circulation and the greater area exist. At about this stage, then, the clot is reduced in volume and is undergoing organization. It consists essentially of a moist, gluey weld of extraordinary adhesiveness. The new growth of vessels is horizontally¹² inward and no doubt horizontally outward from the medulla, providing, of course, in the case of the latter, that the injury has not entailed the destruction of the blood supply of the medullary cavity. Kolodny believes that "the endosteum is not able to participate in the callus formation until the intraosseal blood circulation recovers by formation of an anastomosis between the central portion of the nutrient artery and the metaphyseal blood vessels."⁸

EFFECT OF CUTTING THE VEINS AND LYMPHATICS AT THE SITE OF FRACTURE

The same shearing force that cut the arteries also must cut the veins and lymphatics, and as reposition of the fragments is practically never so accurately made as to bring the cut ends of the vessels into venous alignment, the flow of venous blood and lymph will not be reestablished across the fracture in the vessels except by the probable development of new vessels; however, this will not interrupt the carrying capacity of the veins and lymphatics, as will appear. While the cut arterial vessels are thrombosed to their nearest functioning collateral, the veins seldom are. The venous circulation has for its motivation: (*a*) the propulsive power of the heart, (*b*) the compressive effect of muscle action and (*c*) the suction from the thorax and the heart itself.¹³ The propulsive power of the heart on the venous column, slight in any case, is of course nonoperative in the cut vessels, but the suction from the thorax and heart and the pressure of surrounding parts are still present. The valves in the veins and lymphatics prevent any flow of venous blood or lymph in any direction except toward the heart. Smaller veins (of less than half an inch, such as lie in bone) do not have valves.⁷

INCOMPRESSIBILITY OF MUSCLE TISSUE AND THE PROBABLE EFFECT OF THIS ON THE CIRCULATION OF BLOOD TO A FRACTURE AREA

There can be no doubt concerning the relative incompressibility of muscle tissue. Only by great pressures (those tremendously in excess of any existent in the body) can any compressibility be demonstrated.

12. Wieder, Henry S.: *Regeneration of Bone*, Univ. Penn. M. Bull., 1907, p. 33.

13. Tigerstedt, R.: *A Testbook of Physiology*, ed. 3, New York, D. Appleton & Co., 1906, p. 19. Starling, E. H.: *Principles of Human Physiology*, ed. 4, Philadelphia, Lea & Febiger, 1926, p. 872.

THE LAYING DOWN OF LIME SALTS

The deposition of mineral salts to form hard bone involves a different group of phenomena from those under consideration in this article. The theory that the osteoclasts and osteoblasts have the particular property of tearing down and building up bone does not have the universal recognition today that it did ten years ago,¹⁷ although many writers still accept it. It has been shown that the formation of new blood vessels is mostly horizontal, and that the new trabeculae are arranged in the same direction. Ely¹⁸ and later Blaisdell and Cowan⁶ found, in their experiments on animals, that new bone was first laid down in the angle formed by the bone and the raised periosteum. This is the place where one would expect that anastomosis would first take place between the periosteal circulation and that in the cortex of the bone. It is also the place where the effect of motion between the fragments would be minimized as being farthest from the place of shearing action.

DEVELOPMENT OF FIBROUS TISSUE

The result of the failure of bony union, with all it implies concerning the impossibility of reconstruction of the architecture of the normal bone, is a fibrous union between the fragments. The fact has been mentioned that granulation tissue replaces the blood clot following a fracture. Granulation tissue develops ordinarily into fibrous or scar tissue. In a small wound, this development will take place quickly and almost at the same time throughout the small area; but in a large wound, the process will be progressive and farthest advanced at the place where the granulation tissue started to bud or form. In the case of most large wounds, this will be at the periphery so that the progressive healing is from without inward, or as J. Renfrew White¹⁹ put it, centripetally. In the case of a fracture, there are two bases from which the granulation tissue may start to form; these are the outer periphery of the clot, with which the periosteum is usually associated, and the medullary region, providing, in the case of the latter that the blood supply to this region has not been stopped. With a proper clot and no interruption to its vascularization and the laying down of mineral salts, bone healing will be carried out. When interruption of the continuity of the vessel system takes place,

17. Eising (footnote 10, third reference). Arey, L. B.: The Origin, Growth and Fate of Osteoclasts and Their Relation to Bone Absorption, *Am. J. Anat.* 26: 315, 1919-1920. Watt, J. C.: Deposition of Calcium Salts in Areas of Calcification, *Arch. Surg.* 10:990 (May) 1925. Bancroft, F. W.: Bone Repair Following Injury and Infection, *Arch. Surg.* 5:646 (Nov.) 1922.

18. Ely, L. W.: Experimental Study of the Healing of Fractures, *Arch. Surg.* 5:527 (Nov.) 1922.

19. White, J. R.: Chronic Traumatic Osteomyelitis, New York, Paul B. Hoeber, 1919, p. 28.

direction; this, of course, is toward the heart and away from the fracture. It may also be remembered that the venous and the lymph streams are subject to a suction action by the thorax and heart. It would seem not unreasonable to presume that these factors acting together might create a negative pressure in the venous lymphatic channels in the bone, sufficient to carry off waste products, even if of little magnitude. There is plenty of evidence that in the tearing down process of the old bone, the products are carried away by the old vessels, that is, those running in a vertical direction. As evidence of this, there are the clear vertical spaces (erosion) shown in the old bone; one sees this in the cuts of sagittal sections of repairing bone, and it has been shown particularly in many articles on the subject of bone repair, for example, by Johnson,⁶ by Todd and Her,¹⁵ by Wieder¹² and by others. The eburnation so regularly (though not invariably) seen in cases of nonunion would seem to be a point in favor of believing that in these cases resorption of bone salts and other substances is through the veins and lymphatics.

RELATION OF NEW BONE TRABECULAE TO BLOOD VESSELS

The arrangement of the new trabeculae at the zone of fracture is at right angles to the cortex rather than parallel to it as in normal bone. This is presumably due to the fact that, in general, the new blood vessels growing into the original granulation tissue were derived from the surrounding soft tissues outside the bone and from the medullary cavity. The realignment of the vessels of the cortex is not complete for a year or more after the injury.³ Delafield and Prudden, speaking of the ossification of osteophytes, said:

The blood vessels from which the pathological bone develops grow out of old vessels, and as in the formation of granulation tissue, are irregularly arranged and are subject to a variety of nutritive conditions, so that new bone is usually formed, not in a series of definite lamellae but in a series of irregular spicules or masses.¹⁶

Blaisdell and Cowan⁸ have stated: "The manner of branching and the position of the blood vessels determine the form, position and manner of continuity of the early trabeculae." The progressive change in the direction of the trabeculae from the horizontal to the vertical is probably due to gradual changes in the anastomotic formation of the blood vessels (particularly of the arteries) by virtue of which they (the trabeculae) tend to conform to the direction of the vessels of the bone as a whole.

15. Todd, T. W., and Her, D. H.: *The Phenomena of Early Stages of Bone Repair*, Ann. Surg. 86:715, 1927.

16. Delafield, Francis, and Prudden, T. M.: *A Textbook of Pathology*, ed. 12, New York, William Wood & Company, 1923, p. 1059.

exigencies of the process. Repeated injury to this delicate anastomotic network through motion of the fragments makes necessary repair by the formation of new vessels; this involves retardation in the interior of the callus while at the periphery granulation tissue is progressing to fibrous tissue; the latter contracts in due time and thus reduces the flow of blood to the interior of the callus. As a result, there is delayed or fibrous union.

Since muscle tissue is incompressible (by ordinary pressures), the addition of the volume of the hemorrhage and inflammatory exudate may reduce the lumen of the arterial supply either directly or indirectly by the transmission of pressures throughout adjacent muscles in accord with well known laws of hydraulics.²⁰ This is particularly likely to occur in the presence of resistance to expansion or swelling from fascial planes and circular bandages or casts.

The circulation through the veins and the lymphatics is of equal importance to that in the arterial system, because through their medium the old structure is torn down or resorbed, thus permitting the growth of new vessels to form and establish anastomoses which are essential to bone repair. Interruption to the flow of venous blood and lymphatic fluid by the same pressure that may retard the arterial supply does not occur because a generalized pressure on the veins and lymphatics forces their contained fluid toward the heart.

CONCLUSIONS

Whether or not there are any systemic causes for delayed union and nonunion of fractures, there would seem to be ample reason to believe that the consistent use of methods of treatment of fractures that require (1) good apposition, (2) adequate provision for expansion of surrounding structures and (3) freedom from any shearing or hinge motion between the fragments will be rewarded by a much lessened morbidity percentage. Good apposition is, of course, routine and needs no word of defense. Ample provision for expansion is not always provided in the cast, splint or other device used. Too much emphasis cannot be laid on the importance of splitting or bivalving the cast or in maintaining a constant watchfulness over circumferential bandages that they may never be too tight. A bandage may be correct at the time of its application, but over night, from the restlessness of the patient or from his having had the injured part in a dependent position, the limb may have swollen until the bandages are tight.

Much can be done at the first dressing to prevent excessive hemorrhage and inflammatory reaction. Usually at this time one is dealing

20. King, H. W., and Wisler, C. O.: *Hydraulics*, New York, John Wiley & Sons, 1922, p. 7.

however, the normal bone repair will be interrupted or fail completely, and the characteristic fibrous union will occur. It has been said that the granulation tissue leading to vascularization starts on the periphery of the clot and possibly in the medullary cavity. From these places it is progressively inward and outward. The horizontal series of new arterial vessels may have its continuity interrupted by cutting from the shearing action of the two fragments if moved, and in practice this is done by too frequent or not sufficiently gentle, firm handling in dressing, or it may occur from lack of proper support by the splint, the adjustment of which may permit hingelike motion between the fragments. I cannot see any reason for the belief held by some that "a little motion is good for a fracture"; by this is not meant the gentle contractions of muscle, as, for instance, the motion by the fingers in a forearm fracture, the effect of which is to accelerate the supply of blood to the fracture and to facilitate the elimination of waste by the veins and lymphatics.

If the continuity of the vessels is broken, it will not stop the normal histologic progress of granulation into fibrous or bone tissue at the periphery of the healing area, but only in the newly injured area between the fragments; therefore, the development of granulation into fibrous and perhaps even bone tissue will continue here (at the periphery), while the central area must have its vessel system repaired before it can again take part in the normal process of repair, namely, vessel formation, laying down of lime salts, etc. The inevitable tendency of granulation tissue is to form fibrous tissue, which contracts and deprives this central area of its blood supply; without this, it cannot make the necessary repair of its continuity. No doubt, occasional damage to the new vessels between the fragments is repaired without prejudice to the final result, but if such damage is repeated too often, it may result in deprivation of blood supply to this area through the gradual occlusion of the peripheral vessels of the callus by the formation of fibrous tissue.

SUMMARY

The deposition of lime salts incident to the repair of a fracture is dependent on an adequate circulation in the callus.

Following a fracture, a new set of arterial vessels transverse to the long axis of the (long) bone is developed. These vessels arise by a process of budding, starting, for the most part, at the periphery of the injured area; it must be admitted, however, that in the absence of obstruction to the medullary vessels, such budding may also arise from them. An anastomotic arterial system is thus established, and through its medium the trabeculae are laid down, at first transverse to the long axis of the (long) bone but later obliquely and eventually vertically, as is normal, this being brought about by the ever changing anastomoses of the vessels. The lime salts are removed and replaced according to the

STUDIES IN INTESTINAL OBSTRUCTION

IV. STRANGULATION OBSTRUCTION: A COMPARISON OF THE TOXICITY OF THE INTESTINE AND OTHER TISSUES AUTOLYZED IN VIVO AND IN VITRO *

OWEN H. WANGENSTEEN, M.D., PH.D
AND
GEORGE W. WALDRON, B.S.
MINNEAPOLIS

In both the patient and the experimental animal, strangulating types of obstruction are the most serious. In addition to the occlusion of the bowel in strangulation obstruction a segment of intestine is deprived of its blood supply. The poorer prognosis and quicker fatal issue in such instances are due to the injury of the strangulated loop.

A study of strangulation obstruction, therefore, resolves itself into an inquiry into the autolysis of injured segments of intestine. It has been demonstrated in another study¹ that segments of intestine deprived of their blood supply undergo a rapid autolysis, with the liberation of toxic substances. In a few dogs in which strangulation obstructions had been established and the strangulating mechanism released a few hours later, death occurred, apparently caused by the absorption of toxic bodies from the strangulated segment. Autolysis of the segment to which the blood supply had been interrupted, rather than absorption from the lumen of such a segment, appeared to be responsible for the fall in blood pressure and the lethal issue observed in such animals on releasing the constriction of the strangulated segment.

In this investigation, comparisons have been made of the toxicity of various tissues when deprived of their blood supply. A study of the nonprotein nitrogen of the blood and urine has also been made in a number of these animals to note whether the autolysis of devitalized tissue would provoke the same alterations in the chemistry of the blood and urine as are observed in simple occlusion of the upper part of the intestine. An effort has also been made to ascertain whether the subcutaneous administration of sodium chloride to animals in the peritoneal cavities of which tissues were allowed to autolyze afforded the animal any protection.

* From the Department of Surgery of the University of Minnesota.

* Presented before the Minnesota Pathological Society, April 19, 1927.

1. Wangenstein, O. H., and Loucks, M.: Studies in Intestinal Obstruction: II. The Absorption of Histamine from the Obstructed Intestine, Arch. Surg. 16: 1089 (May) 1928.

with the break before the muscles have become spastic; there is only moderate swelling, and replacement of the fragments may be possible. The part should be placed in the position of election. Thus a fracture of the elbow if seen shortly after its occurrence may be placed in acute flexion with little danger of excessive swelling subsequently, and in fractures of the lower leg, the foot may be turned in. It is unnecessary and contributory to excessive swelling for one to endeavor to make an exact diagnosis by manipulation; roentgen-ray examination should follow the first dressing as soon as possible and readjustment of any deformity shown may then be made as soon as convenient, after which the roentgen ray should be employed to verify the position of fragments.

The fracture appliance, of whatever type, should not permit of any motion of the bone at the site of the fracture. The old rule to splint the proximal and distal joints is a good one.

Fractures should not be dressed frequently, unless the cause is imperative, and in dressing should be handled firmly and gently so that there is no motion between the fragments.

Open operations should be so planned and conducted as to minimize the damage to the surrounding circulation. The use of a tourniquet is not advisable, since with it, one is not cognizant of the amount of damage being inflicted on the circulation. Fibrous tissue about the fragments should be removed and likewise eburnated bone which is too compact to permit formation of new vessels with the consequent anastomotic phenomena so important in repair of fractures.

weight being 63.5 Gm. The average weight of the dogs into the peritoneal cavities of which loops of bowel were placed was 37 pounds (16.8 Kg.). The dog that recovered weighed 25 pounds (11.3 Kg.) and the segment of intestine, 52 Gm.

The four dogs into the peritoneal cavities of which pieces of liver were placed died. In one animal, the small lobe of the liver near the gallbladder was detached and dropped into the peritoneal cavity; at autopsy, there was no indication that bleeding had occurred from the liver. In the other animals, the pieces of liver used were obtained under sterile precautions from normal dogs killed during the course of another experiment. Three of these dogs weighed 35 pounds (15.9 Kg.) and the other 25 pounds. The weight of the segments of liver used averaged 56 Gm. One animal into the peritoneal cavity of which 35 Gm. of liver was placed, lived five days. The other three animals survived a little less than twenty-four hours. Three of the four dogs were given saline solution subcutaneously.

Of twelve dogs in which the animal's own spleen was detached from its source of blood supply and dropped into the peritoneal cavity, eight died and four recovered. The weights were not obtained in some of these animals, but there did not appear to be any uniformity between the size of the spleen, the weight of the dog and recovery. One animal weighing 26 pounds (11.8 Kg.) recovered following detachment of a spleen that weighed 82 Gm. Another dog that weighed 21 pounds (9.5 Kg.) died two days following the detachment of its spleen, the weight of which was only 22 Gm. Six dogs were given salt solution subcutaneously. One dog was given water subcutaneously. Post-operative treatment was not given to the remaining five animals. Of the four dogs that recovered, all were given saline subcutaneously. The average length of survival following the operative procedure on the other dogs was three and a half days.

A kidney removed from other healthy dogs was placed in the peritoneal cavity of two dogs, each weighing 25 pounds. The weights of the kidneys used were 34 and 29 Gm., respectively. One of these dogs died eighteen days later from a suppurating abdominal wound; the other dog made a permanent recovery. Two kidneys were placed in the peritoneal cavity of a third dog. The combined weight of the two kidneys was 60 Gm. This dog also survived the procedure. The employment of tissue obtained from another animal did not seem to be of any special handicap in recovery.

In order to establish better quantitative comparisons of the toxicity of various tissues in the process of autolysis, pieces of tissue weighing from 30 to 60 Gm. were removed under sterile precautions from two dogs killed with ether. The pieces were placed in sterile bottles with wide mouths containing about an equal weight of physiologic sodium

METHOD

All surgical procedures were performed under ether anesthesia and aseptic technic. Blood was obtained from the jugular vein or the vein on the outer aspect of the hind leg of the dog. The blood urea was determined according to the method of Van Slyke and Cullen² and the blood chlorides after the method described by Gettler.³ A number of the animals were kept in metabolism cages. The urine was collected and the nonprotein nitrogen determined by the micro-Kjeldahl method of Folin and Denis.⁴ When sodium chloride was given, it was administered subcutaneously with a 50 cc. syringe; 400 cc. of a 2 per cent sodium chloride solution being given once daily. Segments of small intestine about a foot or a little more in length, weighing from 46 to 75 Gm., were removed from one dog and placed in the peritoneal cavity of another. In four instances, the loop was irrigated successively with water, alcohol, ether and water, until the contents were returned clear. About 2 liters of fluid were used in the irrigation of each loop. A large needle was inserted in one end, and the other end was left open. Irrigation was performed with a 50 cc. syringe. A few inches of both ends of the segment of intestine, where the irrigation was less effective, were cut off before the remainder of the segment was deposited in the peritoneal cavity of the other dog. In the other eight instances, following this irrigation, the bowel was slit on its antimesenteric border and the mucous surface painted with phenol in certain areas in order to destroy the mucous membrane. The destroyed mucosa was then scraped off with a knife. In a few instances, a major part of the mucosa was stripped off in this manner leaving only islands here and there.

The spleen was detached from its blood supply and dropped into the free peritoneal cavity in a number of animals. The same procedure was carried out with pieces of liver. The pancreas excised from other dogs was placed in the peritoneal cavity in two animals, and in a few animals kidneys excised from other dogs were used in the same way.

The twelve dogs from which segments of intestine were removed recovered following the establishment of the continuity of the intestinal tract by lateral anastomosis. Death occurred in eleven of the twelve animals into the peritoneal cavities of which the twelve segments of intestine were deposited. One dog recovered; in this animal, a good portion of the mucosa had been removed. Another animal lived seven days. Five dogs survived the procedure two days. The others died on the day following operation. One of the latter died in convulsions, a mode of death not uncommon in the rats injected intraperitoneally with the intestinal contents of either a dog or a rabbit. Two of the dogs that were given salt solution subcutaneously died the day following the placing of the intestinal loop into their peritoneal cavities. The heaviest segment of intestine weighed 75 Gm., the lightest 46 Gm., the average

2. Van Slyke, D. D., and Cullen, G. E.: A Permanent Preparation of Urease and Its Use for Rapid and Accurate Determination of Urea, *J. A. M. A.* **62**:1558 (May) 1914.

3. Gettler, A. O.: A Method for the Determination of Death by Drowning, *J. A. M. A.* **77**:1650 (Nov.) 1921.

4. Folin, O., and Denis, W.: Nitrogen Determinations by Direct Nesslerization; I. Total Nitrogen in Urine, *J. Biol. Chem.* **25**:473, 1916.

placed in the peritoneal cavity. In the body cavity the rate of autolysis would be somewhat increased because of the simultaneous action of living tissue in aiding the disintegration of the dead tissue. Table 1 shows the results of such injections, the results checking closely with those obtained previously when the same tissues were placed in the peritoneal cavity.

COMMENT

When the loops of the bowel removed from one dog and made bacteria-free by mechanical cleansing and irrigation with antiseptic solutions are placed in the peritoneal cavity of another animal, death quickly supervenes as a consequence of autolysis of the segment of intestine deprived of its blood supply. Such segments of bowel, averaging 63.5 Gm. in weight, were placed in the peritoneal cavities of twelve dogs. Only one recovered; in this animal, a considerable portion of the mucosa had been scraped off. In two animals, a portion of the mucosa was removed from the segment of bowel, and each of the dogs into the peritoneal cavities of which the prepared segments of bowel were placed was given 400 cc. of a 2 per cent sodium chloride solution subcutaneously. Both dogs died the next day.

Four dogs died after pieces of liver averaging 56 Gm. were placed in the peritoneal cavities. A salt solution was given subcutaneously to three of these animals, but without avail.

Kidney tissue removed from other dogs was placed in the peritoneal cavity of three dogs. One death occurred eighteen days later from a suppurating abdominal wound; the other two animals recovered. Saline solution was not given to any of these animals.

Death occurred in eight of the twelve dogs in which the spleen was detached from its source of blood supply and dropped into the peritoneal cavity. Six of the twelve dogs were given salt solution subcutaneously; the four dogs that recovered belonged to this group. The five dogs to which salt solution was not given subcutaneously died, as did the animal given water subcutaneously.

The postmortem pictures of the animals that died following deposition of segments of intestine and pieces of spleen or liver in their peritoneal cavities were much the same. Three or four hundred cubic centimeters of a brownish or serosanguineous fluid was usually present, and the peritoneal surfaces were reddened. The tissue placed in the peritoneal cavity could frequently not be identified other than as a friable, mushy mass. When the animal died the day after the operative procedure, or on the following day, the tissue was often spongy and contained gas. A fibrinous-like exudate was found uniformly about the tissue introduced. Cultures were made in several instances. In a number of these cultures *B. coli* were grown.

chloride, and the bottles were then placed in the incubator. At twenty-four, forty-eight, seventy-two and ninety-six hours following the incubation, a few cubic centimeters of fluid was aspirated from the bottles and injected intraperitoneally into rats. A sufficiently large number of

TABLE 1.—*Results of Injection of Autolyzed Tissue After Sterilization*

| Tissue | Hours Incubated | Amount Injected, Cc. | Result | Remarks |
|----------|-----------------|----------------------|----------|---|
| Kidney | 24 | 18 | Recovery | Mildly ill |
| | 48 | 12 | | Died 2 days later |
| | 48 | 10 | Recovery | Fairly ill |
| | 72 | 5 | Recovery | Stuporous, but recovered |
| | 96 | 10 | Died | Mildly ill after injection; died 2 days later |
| | 4 months | 4 | Died | Convulsions 10 minutes after injection |
| Spleen | 24 | 15 | Recovery | Mildly ill |
| | 48 | 12 | Recovery | Mildly ill |
| | 48 | 10 | Recovery | Mildly ill |
| | 72 | 5 | Recovery | Stuporous, but recovered |
| | 96 | 10 | Died | In convulsions 5 minutes after injection; convulsive seizures for 45 minutes; died next day |
| | 4 months | 4 | Died | Very ill; died during night |
| Liver | 24 | 15 | Died | Moderately ill; died during night |
| | 48 | 12 | Died | Moderately ill; died during night |
| | 48 | 10 | Recovery | Fairly ill |
| | 72 | 5 | Died | Stuporous; found dead in a.m. |
| | 96 | 10 | Died | Not as ill as other animals injected with 4 day tissue culture; died 2 days later |
| | 4 months | 4 | Died | Stuporous; died 12 minutes later |
| Pancreas | 24 | 15 | Died | Dead 20 minutes after injection |
| | 48 | 12 | Died | Died during night |
| | 48 | 10 | Died | Died during night |
| | 72 | 4 | Recovery | Stuporous following injection |
| | 96 | 10 | Died | Moderately ill after injection; died 2 days later |
| | 4 months | 4 | Died | Convulsions; dead in 5 minutes |
| Duodenum | 24 | 17 | Died | Dead 30 minutes after injection |
| | 48 | 12 | Died | Died during night |
| | 48 | 10 | Died | Died during night |
| | 72 | 5 | Died | In convulsions 3 minutes after injection; dead 2 minutes later |
| | 96 | 10 | Died | Convulsive seizures; dead a few minutes after injection |
| | 4 months | 4 | Died | Very ill; dead in 30 minutes |
| Jejunum | 24 | 15 | Died | Dead 7 minutes after injection |
| | 48 | 12 | Died | Very ill; died a few hours after injection |
| | 48 | 10 | Died | Very ill; died a few hours after injection |
| | 72 | 5 | Died | Stuporous; died during night |
| | 96 | 10 | Died | Convulsive seizures; dead 10 minutes after injection |
| | 4 months | 4 | Died | Convulsions; died in 10 minutes |
| Stomach | 24 | 18 | Died | Dead 7 minutes after injection |
| | 48 | 12 | Died | Very ill; dead a few hours after injection |
| | 48 | 10 | Died | Very ill; dead a few hours after injection |
| | 72 | 5 | Recovery | Stuporous, but recovered |
| | 96 | 10 | Died | Convulsive seizures; dead 4 minutes after injection |
| | 4 months | 4 | Died | Very ill; died in 20 minutes |
| Muscle | 24 | 15 | Recovery | Mildly ill |
| | 48 | 12 | Died | Died during night |
| | 48 | 10 | Died | Died during night |
| | 72 | 5 | Recovery | Stuporous, but recovered |
| | 96 | 10 | Died | Lethargic and stuporous; died during night |
| | 4 months | 4 | Died | Convulsions; dead in 12 minutes |

bottles were prepared so that each day's injection was made from a separate bottle. Injections of tissues autolyzed in this manner were made with liver, spleen, pancreas, muscle, kidney, stomach and intestine.

In the incubator, tissues would undergo about the same qualitative process of autolysis as the same tissue deprived of its blood supply when

TABLE 2.—*Toxicity of Various Tissues in Process of Autolysis*

| Dog | Nature of Procedure | Day After Operation | Blood Mg. per 100 Cc. | | Urine and Vomitus* | |
|---|--|---------------------|-----------------------|-----------|--------------------|---------------------|
| | | | Urea | Chlorides | Amount | Nonprotein Nitrogen |
| 55 | Spleen detached from blood supply 10/4/26; no saline | 0 | 16.80 | 480 | | |
| | | 1 | 14 | 390 | | |
| | | 2 | 14.54 | 410 | | |
| | | 3 | 10.20 | 430 | | |
| | | 4 | 20.53 | 400 | | |
| | | 5 | 23.03 | 300 | | |
| Dog died 10/9/26 | | | | | | |
| 59 | Spleen detached from blood supply 10/12/26; 400 cc. 2% sodium chloride given once daily | 0 | 15.80 | 430 | | |
| | | 1 | 15.40 | 450 | | |
| | | 2 | 12.00 | 430 | | |
| | | 3 | 13.00 | 530 | | |
| | | 4 | 17.73 | 400 | | |
| | | 5 | 11.20 | 430 | | |
| | | 6 | 14 | 400 | | |
| | | 7 | 20.53 | 510 | | |
| | | 8 | 15.80 | 530 | | |
| | | 9 | 13.06 | 510 | | |
| | | 10 | 14.03 | 300 | | |
| | | 11 | 14.47 | 310 | | |
| Dog well | | | | | | |
| 118 Weight, 25 pounds (11.3 Kg.) | 52 Gm. of intestine put into the peritoneal cavity 2/1/27; no saline | 0 | 13.06 | 400 | | |
| | | 1 | 10.80 | 330 | 550 | 4.67 |
| | | 2 | 15.80 | 400 | 1,470 | 5.35 |
| | | 3 | 10.30 | 400 | 1,900 | 7.06 |
| | | 4 | 17.20 | 430 | 1,000 | 6.40 |
| | | 5 | 15.80 | 330 | 1,070 | 4.68 |
| | | 6 | 13.30 | 390 | 1,310 | 5.49 |
| | | 7 | 10.50 | 300 | 1,230 | 5.66 |
| | | 8 | 15.37 | 410 | 700 | 3.26 |
| | | 9 | 17.02 | 380 | 450 | 2.48 |
| Dog recovered | | | | | | |
| 121 Weight, 30 pounds (13.6 Kg.) | Two kidneys (60 Gm.) put into the peritoneal cavity 2/10/27; no saline | 0 | 10.20 | 400 | 120 | 1.14 |
| | | 1 | 15.80 | 490 | 375 | 2.62 |
| | | 2 | 14.73 | 300 | 1,320 | 7.58 |
| | | 3 | 11.20 | 430 | 1,550 | 5.81 |
| | | 4 | 24.26 | 440 | 1,100 | 0.34 |
| | | 5 | 13.30 | 410 | 900 | 5.76 |
| | | 6 | 10.53 | 390 | 700 | 5.32 |
| | | 7 | 14.78 | 420 | 520 | 4.03 |
| | | 8 | 17.33 | 330 | 580 | 3.23 |
| | | 9 | 15.24 | 430 | 340 | 2.30 |
| Dog well | | | | | | |
| 117 Weight, 35 pounds (15.9 Kg.) | 15 inch closed loop obstruction; continuity reestablished by lateral anastomosis 2/9/27; no saline | 0 | 9 | 420 | 100 | 1.25 |
| | | 1 | 13.00 | 400 | 1,050 | 4.77 |
| | | 2 | 15.30 | 490 | 2,850 | 5.91 |
| | | 3 | 23.08 | 300 | 1,000 | 5.60 |
| Dog died 2/12/27; loop markedly gangrenous; perforations on antimesenteric border; bloody fluid in peritoneal cavity and in the closed loop | | | | | | |
| 126 Weight, 35 pounds (15.9 Kg.) | 15 inch closed loop obstruction; continuity reestablished by lateral anastomosis 2/14/27; 400 cc. 2% sodium chloride once daily, discontinued on 2/17/27 | 0 | 14.70 | 430 | 110 | 1.02 |
| | | 1 | 12.00 | 410 | 2,300 | 4.40 |
| | | 2 | 16.30 | 420 | 4,700 | 5.95 |
| | | 3 | 10.33 | 390 | 1,900 | 5.36 |
| | | 4 | 14.47 | 040 | 475 | 4.41 |
| | | 5 | 15.40 | 490 | 500 | 4.61 |
| | | 6 | 13.52 | 450 | 340 | 3.27 |
| | | 7 | 20.53 | 440 | 370 | 3.00 |
| | | 8 | 24.20 | 410 | 260 | 2.57 |
| Dog moribund; killed 2/23/27; perforations and extensive gangrene of closed loop | | | | | | |

* The dogs were allowed to drink water. They were starved for one day before being placed in metabolism cage and were not given food while in the cage.

"short circuiting" method for treating subjects with chronic intestinal obstruction. Experimental as well as clinical evidence has shown it to be decidedly unsafe. Perforations have been known to occur years after turning in the ends of such a loop. (Barracz, R.: Experimenteller Beitrag zur Frage der Totalen Ausschaltung mit totalem verschluss der ausgeschalteten Darm-schlinger zugleich Beitrag zur axialen Darmvereinigung, Arch. f. klin. Chir. 58: 120, 1899. Kammerer, F.: Bilateral Exclusion and Occlusion of the Intestine, Ann. Surg. 61:497, 1915. Wiesinger: Zur Darmausschaltung, Deutsche Ztschr. f. Chir. 100:1267, 1909.)

but with no greater regularity from the peritoneal cavity of the dogs in which intestinal segments had been placed than when liver or spleen was used.

In these experiments on the autolysis of various tissues in the peritoneal cavity, the liver and the intestine seemed to be the most toxic. Kidney tissue appeared relatively nontoxic. The disintegrating splenic tissue seemed intermediate in toxicity. The outcome in the dog in which the spleen was allowed to autolyze appeared to be affected favorably by the subcutaneous administration of salt solution. In the instances in which the liver and the intestine were placed in the peritoneal cavity, saline did not appear to have any value. It must be pointed out, however, that dogs with segments of intestine or liver in their peritoneal cavities lived only about a day, whereas the animals in which the spleens had been detached from the source of blood supply and which did not receive saline survived for more than three days.

When the autolysis was carried on *in vitro* in the incubator at 37 C. and the autolyzed tissue injected into the peritoneal cavities of rats at varying intervals, results of the same nature were obtained. The kidney and splenic tissues were definitely the least toxic. Bowel tissue, pancreas and liver appeared to be most toxic. The latter tissues seemed to disintegrate into toxic bodies more quickly than kidney and splenic tissue. After four days of incubation, the intraperitoneal injection of splenic tissue into a rat elicited marked symptoms. After four months' incubation, marked symptoms were elicited in all instances on injection. The injected substances appeared about equally toxic. Therefore, there would appear to be a qualitative difference in the toxicity of disintegrating tissues early in the process as well as a difference in the rapidity of autolysis.

Chemical studies of the urine of dogs in the peritoneal cavities of which tissues deprived of their blood supply were allowed to disintegrate showed a markedly increased excretion of nitrogen as was observed in the animals with simple occlusion of the intestine. The marked increase of blood urea nitrogen noted in animals with high intestinal obstruction was not observed in these; only slight increases in the nonprotein blood nitrogen were usually obtained.

Studies of the blood and urine nitrogen were also made in four dogs with irrigated obstructions of the closed loop in which the continuity of the intestinal tract had been reestablished by lateral anastomosis. These animals died from gangrene and perforation of the closed loop.⁵ In three

5. Sixteen of twenty-five dogs with irrigated closed loops on whom Dragstedt and his co-workers experimented lived for some time. Possibly, a longer loop would diminish the danger of gangrene and perforation. At one time it was thought that this was a safe way to dispose of segments of intestine in the

Duval and Grigault,¹¹ studying the disintegration of protein in traumatic shock, observed a moderate increase in the nonprotein blood nitrogen of patients in a state of shock. Aub and Wu¹² obtained only slight increases in the nonprotein nitrogen of the blood in animals suffering from true shock after marked muscle trauma. Hashimoto¹³ obtained moderate increases in the nonprotein nitrogen of the blood in which histamine intoxication followed repeated subcutaneous administration of histamine. Whipple and his co-workers¹⁴ noted the increased urinary excretion of nitrogen following proteose intoxication.

In these experiments when disintegration of the tissue occurred following autolysis of tissue *in vivo*, a marked increase in the excretion of nitrogen in the urine was observed, with only a slight increase of the nonprotein nitrogen of the blood. The low values for blood chlorides noted in dogs with simple obstruction of the upper part of the intestine were not obtained in these animals. The increased urinary excretion of nitrogen is due probably only in a small part to the actual disintegration of the autolyzed tissue; the destruction of the devitalized tissue in all likelihood precipitates the breakdown of other body protein.

In this connection, it is interesting to speculate as to the cause of the marked increase in the blood nonprotein nitrogen observed in animals with simple occlusion of the upper part of the intestine. There is no evidence to indicate that the injury of the kidney is greater in animals with simple obstruction than in those in which tissue is allowed to autolyze. The rapidity with which tissue breaks down following dehydration and loss of chlorides would not alone account for the accumulation of nonprotein nitrogen in the blood, especially as this increase is dissipated by the administration of saline. The giving of saline does not prevent the increased urinary excretion of nitrogen, nor does the nonprotein nitrogen in the urine of these animals given saline seem to be increased over that observed in the animals that do not receive salt. Marshall and Davis¹⁵ have shown that nearly all tissues have about the same urea content as blood. If an increase in the nonprotein nitrogen of the tissues in these animals occurred commensurate with that observed in the blood, if saline actually washed out the increased nonprotein

11. Duval, A., and Grigault, A.: L'intoxications par les plaies de guerre. La retention azotée des blessés, *C. R. de soc. de biol.* **81**:873, 1918.

12. Aub, J. C., and Wu, H.: Studies in Experimental Traumatic Shock: Chemical Changes in the Blood, *Am. J. Physiol.* **54**:416 (Dec.) 1920.

13. Hashimoto, H.: Blood Chemistry in Acute Histamin Intoxication, *J. Pharmacol. & Exper. Therap.* **25**:381 (June) 1925.

14. Cooke, J. V., and Whipple, G. H.: Proteose Intoxications and Injury of Body Protein, *J. Exper. Med.* **28**:223 and 243 (Aug.) 1918; *ibid.* **25**:461 (March) 1917.

15. Marshall, E. K., and Davis, D. M.: *J. Biol. Chem.* **18**:53, 1914.

dogs, isolated loops were similarly irrigated, although the ends were left open and lateral anastomoses made; these dogs recovered. A second operation was performed later on one of these dogs; the ends were found partially sealed. There was free fluid in the peritoneal cavity. The dog died following a free opening of this loop. When extensive gangrenous changes obtain in irrigated closed loops, strangulation of intestine has occurred minus the obstructive factor. In these animals, an increased urinary excretion of nitrogen was obtained, but the high blood urea observed in simple occlusion of the upper part of the intestine was not noted.

Corroboration of the rapid disintegration of strangulated intestine previously noted¹ when a segment was strangulated with its mesentery and the constriction subsequently released was observed when the intestine was allowed to autolyze in vivo in the peritoneal cavity, or when the products of autolysis were injected into the peritoneal cavity of rats after being incubated in vitro. Comparisons made with other tissues showed the products of autolysis of intestine to be markedly toxic. Mann,⁶ in removing the liver in dogs, has observed that when a piece of liver two fingerbreadths in width remained free in the abdomen, the dogs died within sixteen hours. Mason and Davidson⁷ also observed the marked toxicity of liver tissue allowed to autolyze in the peritoneal cavity. None of the fifteen dogs survived in which from 30 to 110 Gm. of liver tissue was placed in the peritoneal cavity. The usual period of survival following the operative procedure was about twenty hours. Only three⁸ of six dogs died in which the spleen used weighed from 23 to 68 Gm. The post-mortem appearance of the peritoneal surfaces following the autolysis of tissue described in this paper was noted by these authors.⁷ They also observed that the fluid present in the peritoneal cavity at death was much less toxic on injection than the autolyzing tissue itself.⁹ Delbet and Karajonopoulos¹⁰ made the same observation on muscle tissue autolyzed in vitro.

6. Mann, F. C., quoted by Mason and Davidson: A Study of Tissue Autolysis in Vivo; I. Blood Changes, Physical and Chemical, *J. Lab. & Clin. Med.* 10:622 (May) 1925.

7. Mason, E. C., and Davidson, E. C.: *J. Lab. & Clin. Med.* 10:622 (May) 1925.

8. Mason, E. C., and Davidson, E. C.: A Study of Tissue Autolysis in Vivo; III. Observations Using the Spleen, *J. Lab. & Clin. Med.* 10:997, 1925.

9. Mason, E. C., and Davidson, E. C.: A Study of Tissue Autolysis in Vivo; 11. A Pharmacological Study of the Toxic Material, *J. Lab. & Clin. Med.* 10: 906, 1925.

10. Delbet and Karajonopoulos: De la toxicite des autolysats musculaires au point de vue du choc, *Bull. Acad. de méd.* 80:13 (July) 1918.

INTESTINAL TUBERCULOSIS CAUSING OBSTRUCTION *

J. R. B. BRANCH, M.D.

PEKING, CHINA

From April, 1927 to April, 1928 eight patients with hyperplastic intestinal tuberculosis with obstruction of varying degrees were operated on in the surgical service of the Peking Union Medical College Hospital. The cases, some of which have been reported in a short article previously published, form the basis of this report.¹

Intestinal tuberculosis associated with pulmonary tuberculosis has long been recognized. The importance of early diagnosis and treatment in this condition has been recently stressed in a monograph by Brown and Sampson.² In 1925, Larimore and Fisher³ reported a series of cases of ulcerative processes in the cecum in which the patients were operated on with encouraging though not brilliant results. In an article on tumors of the secum Erdmann and Clark,⁴ in 1927, reported seven cases of tuberculosis of the cecum and terminal ileum with symptoms of intestinal obstruction. In this series, the pulmonary observations were negative.

FREQUENCY

Probably the most severe cases of pulmonary tuberculosis present some intestinal involvement; lesions are found in the intestinal tract of from 70 to 90 per cent of patients dying of this disease.⁵ These lesions are usually of the ulcerative variety, and in only 25 per cent of them does stenosis or stricture develop;⁶ it is during comparatively recent times that operation has been considered possible in such cases. The hyperplastic and stenosing lesions are more commonly treated surgically. In 100 cases of cecal lesions in which the patients were submitted to operation, Gant found four cases of hyperplastic tuberculosis; in Erdmann and Clark's series of forty-eight tumors of the cecum, seven were tuberculous.

*From the Department of Surgery, Peking Union Medical College.

1. Branch, J. R. B.: The Surgical Treatment of Intestinal Tuberculosis, China M. J. **42**:239 (April) 1928.

2. Brown, L., and Sampson, H. L.: Intestinal Tuberculosis, Philadelphia, Lea & Febiger, 1926.

3. Larimore, J. W., and Fisher, A. O.: Tuberculosis of the Cecum, Ann. Surg. **83**:496 (April) 1926.

4. Erdmann, J. F., and Clark, A. E.: Tumors of the Cecum, Ann. Surg. **85**:722 (May) 1927.

5. Fenwick and Dodwell: Lancet **11**:133, 1892.

6. Read, W. D.: Tuberculosis of Cecum, Northwest Med. **20**:282 (Oct.) 1921; Cecal Pathology, *ibid.* **20**:11 (Jan.) 1921.

nitrogen of the blood, an appreciable increase in the urinary excretion of nitrogen would be observed over that obtained in animals that did not receive saline. Water alone fails to obviate this increase in non-protein blood nitrogen. It would appear that an alteration in the permeability of tissue may occur in these animals such that the rapid dehydration and loss of chlorides incident to the obstruction may permit the accumulation of nonprotein nitrogen in the blood.

In the recovery of the animals following the detachment of the spleen and its autolysis in the peritoneal cavity after the subcutaneous administration of saline, it would appear that saline possesses a protective value in combating the toxemia accompanying the disintegration of tissue. It has been maintained that saline performs such a function in the treatment of burns.¹⁶ In the foregoing experiments, however, factors such as the protective influence of the omentum must be controlled before the recovery of the animal is ascribed to saline alone. Evidence was not obtained that would indicate that the administration of saline was of any value in combating the toxemia that occurred when the intestine was deprived of its blood supply.

SUMMARY AND CONCLUSIONS

Comparisons have been made of the toxicity of intestine and various tissues on autolysis in vivo and in vitro. The products of disintegration of the intestine were found to be markedly toxic when segments of small intestine were allowed to autolyze in the peritoneal cavity or when rats were given intraperitoneal injections of the products of autolysis of intestine from sterile containers kept in the incubator. A marked increase in the urinary excretion of nitrogen was observed in the animals in which various tissues were allowed to autolyze; however, only a slight increase in the nonprotein nitrogen of the blood occurred. The low values for blood chlorides observed in dogs with obstruction of the upper part of the intestine were not obtained in strangulation of the intestine alone (closed loop obstruction with gangrene) when the continuity of the remainder of the intestinal tract was restored. The subcutaneous administration of saline to animals with disintegrating segments of intestine appeared to be valueless.

16. Davidson, E. C.: Sodium Chloride Metabolism in Cutaneous Burns and Its Possible Significance for a Rational Therapy, *Arch. Surg.* 13:262 (Aug.) 1926.

mens showed a coexisting old infection with *Schistosoma* in the cecum and ileum, associated with tuberculosis.

The outstanding feature in all of the cases was a generalized thickening of the entire wall of the bowel with old, healed, scar tissue resulting in stenosis of the lumen; in several cases, the stricture was 5 mm. or

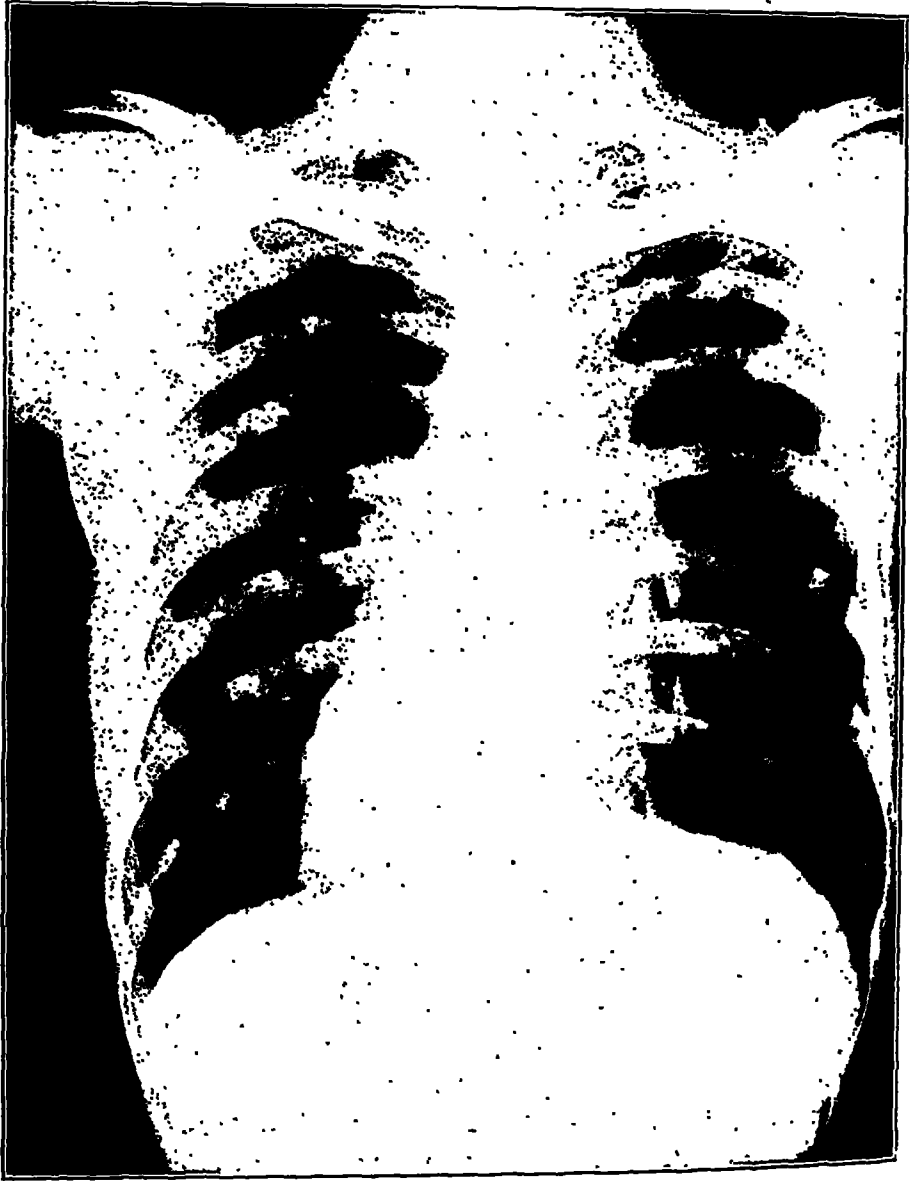


Fig. 1 (case 2).—Roentgenogram of the chest, July 19, 1927, showing thickening of apical pleura on the left side and fibrosed tuberculous infiltration of upper area on the right side. Lesions have not changed in six years.

less in diameter. The mucosa was thickened and often projected into the lumen as papillary elevations, some of them being from 1 to 2 cm. in length. Ulceration was not prominent, though in most of the cases small healed and unhealed ulcers were found. Grossly, little was seen

During the past five years, one of three resections of the right colon performed in this hospital was for tuberculosis. Within the past nine months, seventeen cases of intestinal tuberculosis have been seen on the medical service here, in which the condition was diagnosed by roentgen ray, but for one reason or another the patients were not transferred to the surgical service for operation. Although these figures are not intended to convey any information concerning the relative frequency of the condition in China, it is striking to see so many cases in Peking during one year. I did not encounter a case during twelve years spent in active surgical work in a clinic in Central China, though there must have been many in the community.

PATHOLOGY

About 85 per cent of the involvement in intestinal tuberculosis is in the terminal ileum, cecum and proximal colon.⁷ Fifty per cent of the patients with tuberculous peritonitis have intestinal tuberculosis also, and 20 per cent of the patients having intestinal tuberculosis have peritoneal involvement as well.⁸

The type of lesion varies; in some instances, particularly when associated with pulmonary tuberculosis, it is ulcerative and progressive. This association with processes in the lungs and perhaps elsewhere is responsible for the term "secondary." Another type is the hyperplastic lesion, which is frequently called "primary." While it is true that in the latter variety there may not be any demonstrable tuberculous lesions in the lungs or elsewhere, and that from the data secured by physical examinations and roentgen-ray studies one may fail to find an original focus, it is, however, not only possible but highly probable that there may be or may have been processes elsewhere. Without complete examinations at autopsy, one is not justified in speaking of these cases as "primary."⁹

All of my cases were of the hyperplastic, stenosing variety, and the pathologic pictures were all strikingly similar (fig. 12). The lesions were in the terminal ileum, cecum and ascending colon; in several cases the appendix also was involved in the tuberculous process. Two were associated with tuberculous peritonitis, one in the ascitic and one in the early plastic stage. Three patients had evidence of previous pulmonary tuberculosis, but in only one was the process active. One of the speci-

7. Powell and Hartley: *Diseases of the Lung and Pleura*, Philadelphia, P. Blakiston's Son and Company, 1921, p. 798. Blumberg, Alfred: *Pathology of Intestinal Tuberculosis*, *J. Lab. & Clin. Med.* **13**:405 (Feb.) 1928.

8. Albrecht: *Ueber die Beziehungen zwischen peritoneal und genital Tuberculose*, *Verhandl d. deutsch.*

9. Charbrut, R.: *Sur les resultats de la resection dans la tuberculose ileo-caecale* (40 observations), *J. de chir.* **30**:656 (Dec.) 1927.

in the numerous sections examined. When evidence of dysentery or other probable cause for the lesion is lacking, I am of the opinion, however, that the patient also had intestinal tuberculosis, and the case is accordingly included in this series.

In some instances glandular involvement was observed; it was extensive and marked in one case. The complete report of case 5 is given

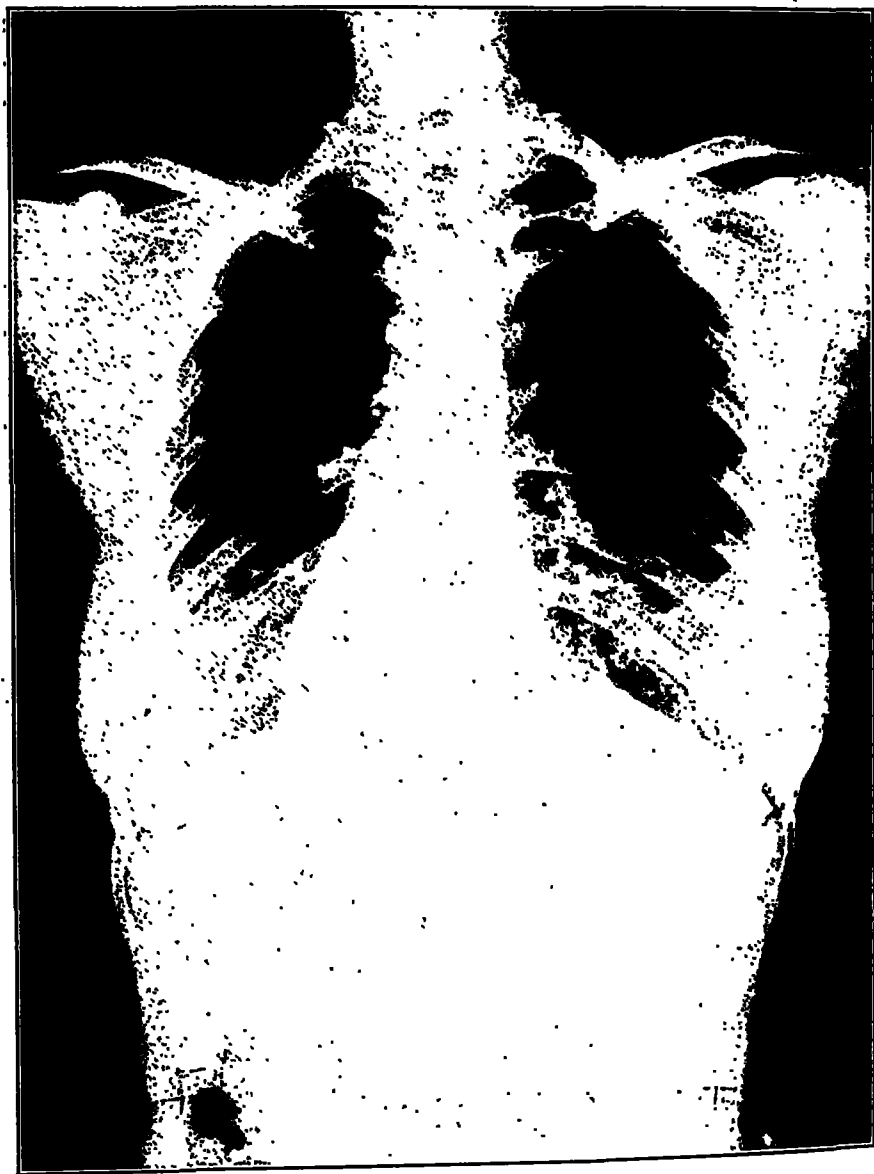


Fig. 3 (case 3).—Roentgenogram of the chest, Sept. 1, 1927, showing essentially normal lungs.

subsequently as typical of the observations in this series; the specimen removed at operation (ileum, cecum and ascending colon) is illustrated in figure 12.

to suggest more than a determined and successful reaction to combat a chronic infectious process, so that the pathologist was disinclined to agree with the clinical diagnosis of tuberculosis until sections were examined. The gross pathologic picture would have been the same if the causative agent had been dysentery, *Schistosoma* or any other chronic



Fig. 2 (case 2).—Roentgenogram, July 19, 1927, made six hours after ingestion of barium, showing dilatation of the terminal ileum, nonfilling of the cecum and incomplete filling of the ascending colon.

irritant. The condition in all cases with the exception of one was diagnosed as tuberculous on microscopic examination, tubercles and bacilli being demonstrated. In case 6, essentially like the others clinically, and with similar gross pathologic changes, tubercle bacilli were not found

showed many small and large papillary growths, varying in length from 0.1 to 1 cm. and in diameter from 0.1 to 0.3 cm. Near the papillary region, namely, in the large intestine, there were several grayish pink and dark red ulcers from 0.2 to 1 cm. in diameter. The mucosa in this region was swollen and elevated, and was a grayish white. The walls of the intestine varied from 0.3 to 2 cm. in thickness.

Sections of the small intestine examined microscopically revealed the irregularly thickened and edematous mucosa with infiltration by polymorphonuclear leukocytes, wandering cells, plasma cells and lymphocytes. Approximately in the center, there was a necrotic and hemorrhagic area which extended even into the submucosa. Elsewhere in the submucosa, marked edema and hemorrhage with infiltration by leukocytes was revealed. The muscularis was thickened in places and at one end showed edema with infiltration by a small number of leukocytes. Opposite the necrotic and hemorrhagic area, the muscularis was replaced by fibrous tissue with small and large blood vessels and infiltration of leukocytes. The serosa was thickened with a large amount of fat tissue and slight infiltration by leukocytes. In the mucosa, submucosa, muscularis and serosa, a few tubercles consisting of epithelioid cells and giant cells were present.

Sections of the large intestine showed that the mucosa was irregularly thickened and edematous with infiltration by wandering cells, plasma cells, lymphocytes and polymorphonuclear leukocytes. In places the submucosa revealed marked edema with infiltration by leukocytes. The muscularis was also irregularly thickened, and at one side areas of small and large intestinal glands were present, some of which were dilated and showed cystic structure, with lumina which were empty or contained a small amount of coagulated material, desquamated epithelium and many polymorphonuclear leukocytes. The muscularis was infiltrated with wandering cells, lymphocytes, plasma cells and polymorphonuclear leukocytes, especially surrounding those areas. Nearly a large tubercle consisting of epithelioid cells and giant cells was present. The serosa was also thickened and edematous with a large amount of fat tissue and infiltration by leukocytes. Sections of surrounding fat and fibrous tissue showed that many small and large tubercles consisting of epithelioid cells and giant cells were present. The tubercles were necrotic in a few places, containing dead cells and polymorphonuclear leukocytes, and were surrounded by lymphocytes and plasma cells. Elsewhere the fat and fibrous tissue also showed infiltration by lymphocytes, plasma cells, polymorphonuclear leukocytes and large cells with granular cytoplasm and oval or round nuclei in the center or near the edge. Here and there, slight hemorrhagic areas were also present. On careful examination only four tubercle bacilli were found. A diagnosis was made of tuberculosis of the cecum with stenosis of the lumen of the intestine.

CLINICAL PICTURE

My experience is similar to that of Erdmann, who stated that the condition in all of his seven cases had been diagnosed at various times as appendicitis. The patient in case 1 was operated on through a McBurney incision for appendicitis when the tuberculous cecum was found; in case 3 the patient had undergone appendectomy four months previously (the appendix was tuberculous); in case 5, exploration had been performed owing to severe, paroxysmal, abdominal pain thought to be due to a strangulated ovarian cyst; in the others, the condition at one time or another was thought to be appendicitis.

REPORT OF CASE

At operation on a Chinese woman, aged 28, a specimen consisting of a portion of the small and large intestines, measuring 19 cm. in length and from 2 to 3 cm. in diameter, was obtained. Gross examination revealed a large amount of grayish, pink and light yellow fat and fibrous tissue attached to the external surface. The cut surface of the large intestine revealed an obstructive portion in which the lumen measured approximately 0.5 cm. in diameter. The mucosa in this region



Fig. 4 (case 3).—Roentgenogram of the colon, June 28, 1927, after injection of barium enema, showing nonfilling of the cecum, general narrowing of the ascending colon at its proximal portion, incompetence of the ileocecal valve and dilatation of the terminal ileum. Diagnosis of a hyperplastic and obstructive lesion (tuberculosis) of the ileocecal region and the ascending colon was made on this examination.

The physical, laboratory and roentgen-ray examinations are more illuminating. In my patients the chest either was normal or, as in three cases, showed old, healed, unimportant pulmonary lesions. In case 7 active lesions were seen. (These observations were confirmed by roentgen-ray films.) The abdominal examination did not reveal anything of importance except in the right iliac fossa; here localized, moderate tenderness was noted, but muscle spasm, involuntary resistance or rigidity was not present. In every case there was a mass in the cecal region which persisted after satisfactory enemas had been given. This mass had the limits of motility one might expect in the cecum, though in case 5 it could be pushed up to the costal margin and down to the pelvis. In one case with associated tuberculous peritonitis, the temperature was

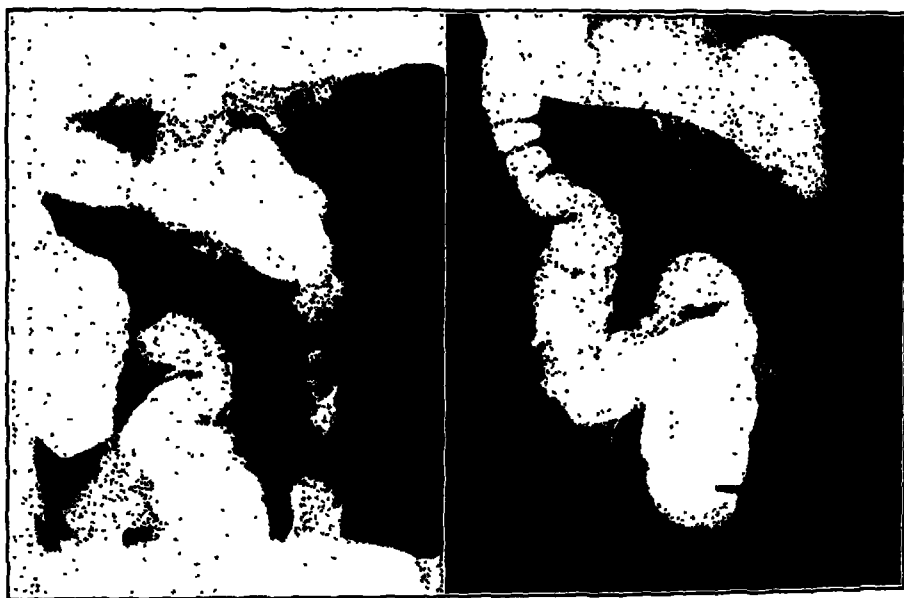


Fig. 6 (case 4).—Roentgenograms, Aug. 31, 1927, made under fluoroscopic control following injection of barium enema, demonstrating the different phases of filling of the cecum and the ascending colon due to active spasm of these parts.

39.2 C.; in another, it was 38.8 C., and in a third uncomplicated case, it was 37.4 C. In the other cases the temperature was normal. The leukocyte count was normal in all but two patients; the patient in case 6 had 11,000 white cells with 86 per cent polyphonnuclears and the patient in case 7 had 14,400 white cells with 74 per cent polymorphonuclears.

The roentgen-ray studies were most important. In all of the cases, with the exception of the first, roentgen-ray examination was made of the intestinal tract. The fluoroscopic and roentgenographic observations were characteristic of either ulcerative or hyperplastic lesion and in every instance, with the exception of case 8, confirmed the clinical diagnosis of intestinal tuberculosis. The constant symptoms were: (1) filling defect—nonfilling, irregularity, narrowing and constriction; (2) gen-

The predominating symptom is abdominal pain, at times general, at other times localized in the right lower quadrant. It is described as colicky, recurrent and paroxysmal, and, in some instances, is exceedingly severe; gurgling of gas is frequently present in the bowels, and in every case there is nausea and vomiting. The attacks of pain in some cases lasted three or four hours, in others as long as seven or eight hours. Most of the patients gave a history of constipation, and some of them had had attacks of diarrhea. In the interim they either were well, or

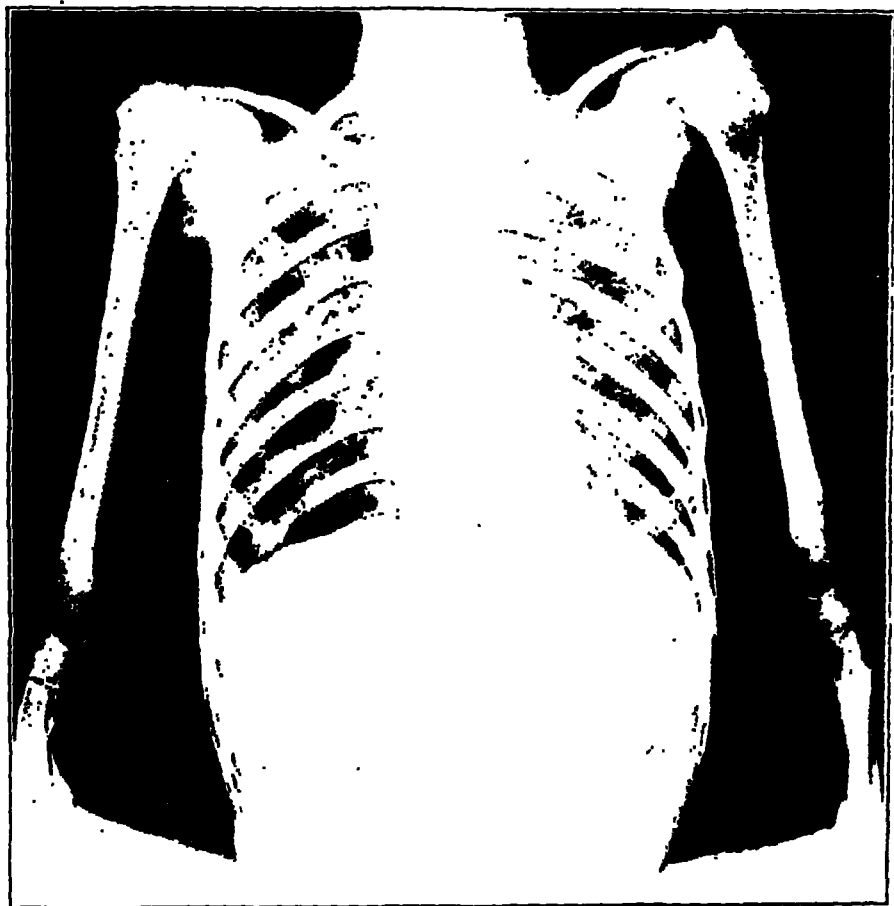


Fig. 5 (case 4).—Roentgenogram of the chest, Aug. 29, 1927, showing moderately increased thickening of the shadows of the hilum on both sides, which, in a subject aged 11 years, was thought to be of some clinical significance.

had vague abdominal discomfort; however, there was a definite tendency for the interval of freedom from attacks to become shorter and for the duration of the attacks to become longer. Such a symptom-complex would seem to indicate a pathologic process in the right lower abdominal quadrant, and one would naturally think first of the most common condition: appendicitis.

methods barium meal proved preferable because it provided the means of studying both the anatomic and the physiologic changes in the intestine, and, therefore, all the diagnostic signs, when present, could be seen. In all five cases in which the barium meal was employed, colonic hypermotility and ileal stasis, the cardinal sign-complex of ulcera-



Fig. 8 (case 5).—Roentgenogram, Nov. 11, 1927, made after the injection of a barium enema, showing filling defect of the cecum and ascending colon, incompetency of the ileocecal valve and dilatation of the terminal ileum.

tion, were present in addition to the filling defect of the cecum and, in some cases, the terminal ileum. Localized tenderness was present in three patients, and a palpable mass which corresponded to the poorly filled cecum was observed in all the patients.

eral colonic hypermotility, and (3) ileal stasis. It may be worth while to mention here that all these observations are but the signs of ulceration or infiltration of the wall of the intestine, and not one of them offers explanation concerning the cause, which should be determined in the light of clinical and laboratory evidence.

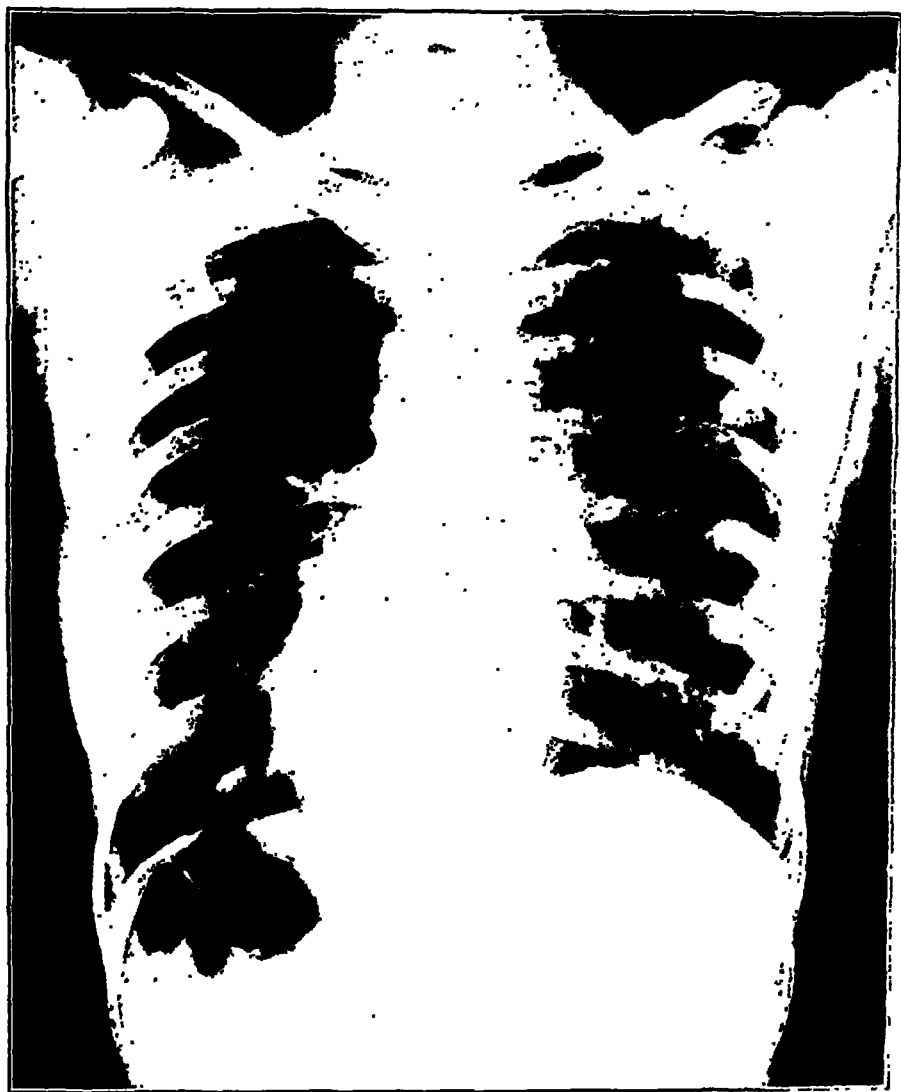


Fig. 7 (case 5).—Roentgenogram of the chest, Nov. 9, 1927, showing fibrotic lesion of lung in first intercostal space area and a calcified mass beneath the third rib near the axilla on the right side. Observations are considered as unimportant.

The greatest amount of information was obtained from examination following both a barium meal and an enema. In one case, the barium enema alone demonstrated the filling defect of the cecum and ascending colon clearly enough for a positive diagnosis to be made. Of the two

Data of Patients with Intestinal Tuberculosis with Obstruction

| Case | Age | Sex | Duration of Symptoms | Previous History of Tuberculosis | Nausea and Vomiting | Pain | Leukocytes | Fever | Lungs | Abdominal Examination | Operation | Complications | Pathologic Observations | Results |
|------|-----|-----|----------------------|----------------------------------|---------------------|------|---|---------|---|---|---|---|---|---|
| 1 | 25 | M | 10 mo. | + | + | ++ | 8,200 | 0 | Latent tuberculosis in both upper lobes | Tenderness and mass in right lower quadrant; no rigidity | Resection of 30 cm. of terminal ileum and cecum; end to side enterocolostomy | Flare up of pulmonary process; superficial infection of incision | Tuberculosis of ileum and cecum, hyperplastic with ulceration | Cured |
| 2 | 30 | M | 5 yr. | + | + | ++ | 6,400-9,100; polymorphonuclears, 57-70% | 0 | Latent tuberculosis in both upper lobes; no advancement in 6 years | Tenderness and mass in right lower quadrant; no rigidity | Resection of terminal ileum, cecum and ascending colon; aseptic end to end enterocolostomy prophylactic ileostomy | Slight superficial infection around enterostomy tube | Tuberculosis and schistosomiasis around terminal ileum, cecum and ascending colon | Cured |
| 3 | 25 | F | 1½ yr. | None | + | + | 4,600-5,300; polymorphonuclears, 68-73% | 0 | Clear | Tenderness and mass in right lower quadrant; no rigidity; small fecal fistula | Extensive tuberculous loss of visceral and parietal peritoneum with ascites | Phlebitis of left femoral vein | Tuberculosis of ileum, cecum, appendix and ascending colon | Well enough to go to school but some vague abdominal discomfort |
| 4 | 11 | F | 7 mo. | 0 | + | + | 8,100; polymorphonuclears, 71% | 39.2 C. | Negative on physical examination; X-ray shows thickening of shadows of the hilum thought to be of some importance | Doughy in consistency, and mass and tenderness in right lower quadrant; no rigidity | Extensive early plastic tuberculous of the visceral and parietal peritoneum | Flare up of pulmonary process; steady decline; intestinal obstruction | No autopsy | Died |

DIAGNOSIS

The two conditions with which one is most likely to confuse these hyperplastic occlusive lesions of the cecum are: appendicitis and malignant growth.

A malignant growth is usually seen in older people; it is most often associated with blood and mucus in the stools, and the symptoms are generally of short duration. My cases were all in young people between 25 and 30 years of age, and a malignant tumor was not probable. During the time in which this series of cases was collected a patient with a malignant growth in the right colon was not encountered.

The difficulty, therefore, has been to exclude appendicitis, and since the first two cases I have been moderately accurate in diagnosis. As already stated, all of my patients were admitted with a provisional diagnosis of appendicitis. If the history and clinical picture aroused suspicion of intestinal tuberculosis, a series of roentgen-ray pictures was made. One must, however, constantly have in mind the danger of this delay if one is dealing with a case of acute appendicitis. Three of my patients subjected to roentgen-ray examination were found to have chronic appendicitis with normal cecums.

If a patient with a suggestive history has a mass in the cecal area, a normal or nearly normal temperature, pulse rate and white blood count, no acute tenderness and no involuntary muscular resistance or rigidity, I have felt safe in carrying on the roentgen-ray studies of the intestine. Hourly counts were made in one case with leukocytosis, and the temperature was closely watched.

In case 8, the clinical diagnosis of intestinal tuberculosis was not confirmed by roentgen-ray studies but was demonstrated at operation; this case was in an early stage; with most of the lesion in the appendix and head of the cecum only. In another case of subsiding appendicitis, the roentgen-ray report indicated a hyperplastic occlusive lesion in the cecum; however, a lesion was not found at operation. With these two exceptions the roentgen-ray studies have not failed to give an accurate idea of the condition.

TREATMENT

Resection of the diseased portion of the bowel with enteroclostomy is the operation of choice; this was done in six cases, with one death and five recoveries resultant. I have developed an aseptic technic based on the method of Scarff,¹⁰ and adapted it to end to side anastomosis; this has been described and illustrated in detail elsewhere.¹¹ Sometimes the

10. Scarff, J. E.: Aseptic End and End Suture of Intestine, *Ann. Surg.* 83: 490 (April) 1926.

11. Branch, J. R. B.: Aseptic Intestinal Anastomosis in Resection of the Large Bowel, *Surg. Gynec. Obst.*, 1928.

terminal ileum is as large as the colon, and end to end anastomosis is done. The patient in case 4 had also extensive tuberculous peritonitis and was not in condition to stand more than an enterostomy to relieve obstruction. The patient in case 7 was also in rather poor condition, and there was extensive and massive involvement of the mesenteric and

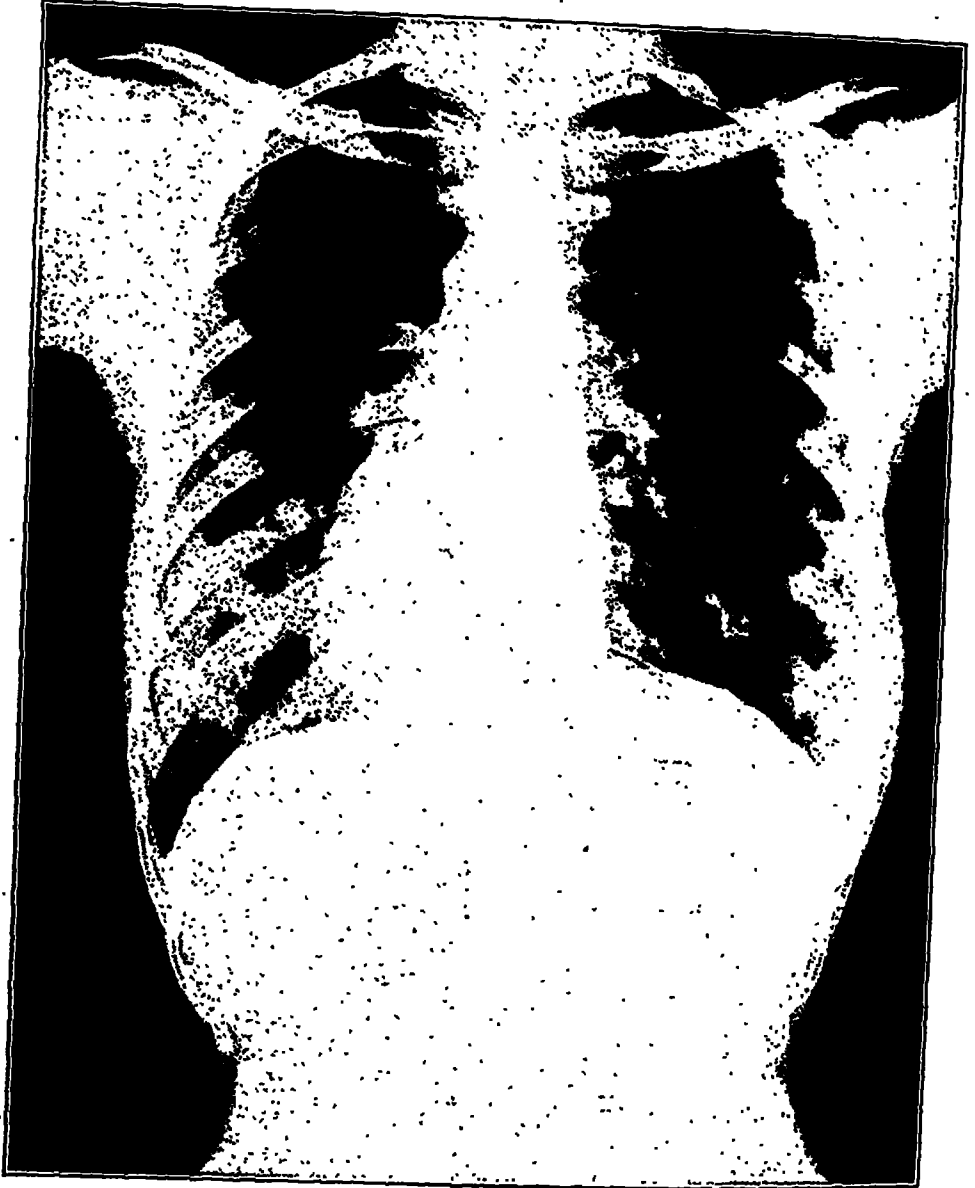


Fig. 9 (case 6).—Roentgenogram of the chest, June 3, 1927, showing normal lungs.

retroperitoneal glands, with caseation and softening; the abdomen, after exploration, was closed, without further treatment. In such a case, the surgeon might consider isolating the diseased portion of the bowel, leaving it in situ, bringing the two cut ends out through the skin, suturing them there and, at the same time, doing an enterocolostomy. When the

| | | | | | | | </ | | | | | |
|--|--|--|--|--|--|--|----|--|--|--|--|--|

ileus and its consequences, and (2) the limiting, for four or five days after operation, of all fluid intake to the subcutaneous and intravenous administration of solutions of physiologic sodium chloride or dextrose. Nothing is given by mouth or rectum, and the liberal use of morphine further helps to reduce peristalsis to a minimum.

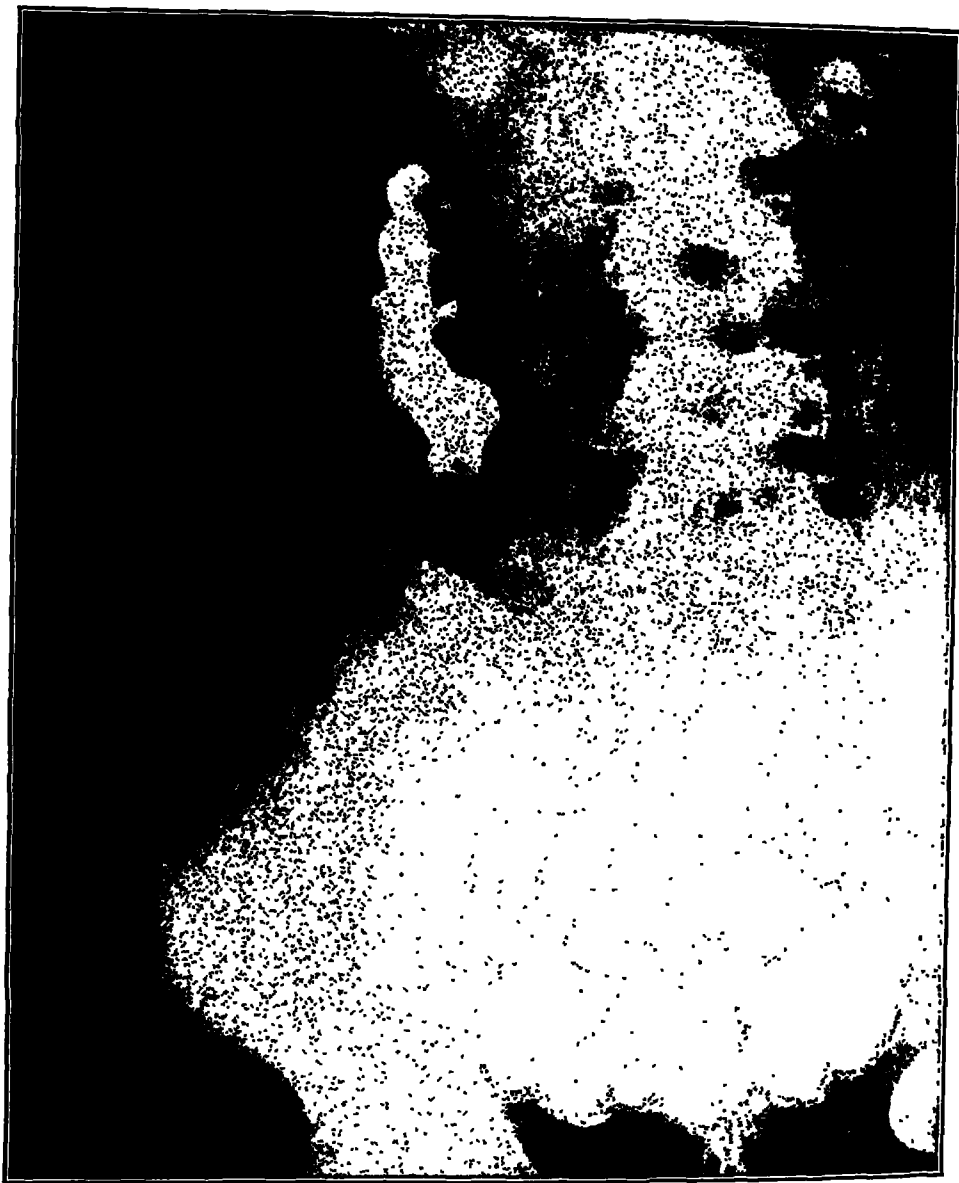


Fig. 11 (case 6).—Roentgenogram, Dec. 7, 1927, made eight hours after ingestion of barium, showing marked ileal stasis. The head of the barium column has reached the descending portion and sigmoid.

RESULTS

It is too early to report end-results in any of my cases. In the first five resections, there was no mortality; in the sixth, the patient died of pneumonia and peritonitis. The autopsy showed a leak at the anasto-

patient's condition permits it, this isolated section, by this time merely a mucous tube freed from the fecal current, may be excised. As the obstruction in my case of this type was not extensive, I decided to try general reconstructive treatment with heliotherapy and, later, resection. A simple short circuiting entero-enterostomy has not proved of great



Fig. 10 (case 6).—Roentgenogram, Dec. 6, 1927, made after the injection of a barium enema, showing no filling of the cecum and dilatation of the terminal ileum.

value. Considerable importance is attached to two features in the operative and postoperative procedure: (1) the prophylactic or compensatory enteroenterostomy suggested by Charles Mayo to avoid possible paralytic

gas per rectum spontaneously, and stools were normal when food was given by mouth. The enterocolostomy openings functioned normally in all cases as shown clinically and by follow-up roentgen-ray examinations. One patient died—the patient in case 4, who had extensive intestinal tuberculosis of the early plastic stage in addition to the intestinal lesion. Emergency enterostomy was performed to relieve intestinal obstruction, and the patient died forty-two days after operation. Five patients are well enough to carry on their usual vocations.

mosis with a resultant peritonitis. The area of cecal involvement was slightly greater than estimated at operation, and not enough of the bowel was resected; the sutures, not being taken in healthy normal colon, sloughed; the patient also had pulmonary tuberculosis and bronchopneumonia. In three resections, some local infection was present in the



Fig. 12 (case 5).—Specimen removed at operation, described in text.



Fig. 1 (case 1).—Tumor of the wall of the chest; the area of density is shown extending from the second to the fourth ribs, near the sternal border of the right side.

MALIGNANT TUMORS OF THE WALL OF THE CHEST

CHARLES D. LOCKWOOD, M.D.

PASADENA, CALIF.

Malignant tumors of the wall of the chest, apart from metastatic carcinoma, are relatively rare. They are usually sarcomatous. Two hundred and thirteen cases were collected by Hedblom¹ in 1921; of these, 61.4 per cent were sarcoma and 18.7 per cent chondroma. Few cases appear in the literature since that time, and in view of the great interest which is now maintained in thoracic surgery, it seems worth while to report two cases in which the patients have been under my care in the past two years.

The pathologic processes of these tumors does not differ from that of sarcoma or chondrosarcoma in other parts of the body. They may take their origin from the soft parts, the cartilage, ribs, sternum, clavicle or scapula. As the growth develops, it invades all of the structures of the wall of the chest and may finally attack the pleura. The two cases here reported began in the cartilaginous portions of the upper ribs near the manubrium.

REPORT OF CASES

CASE 1.—Mrs. K., aged 50, childless, consulted me in November, 1922, concerning a tumor of the wall of the chest beneath the right breast. She first noticed the tumor in April, 1922. It was painless but seemed to be increasing in size. She had gained in weight. Examination revealed a bony-like tumor involving the third, fourth and fifth ribs on the right side near the costocartilaginous junction. It was slightly movable and not tender. The breast was normal; there were no enlarged axillary glands. Stereoscopic x-ray films showed an area of increased density, 8 by 6 cm. between the first and fourth ribs. There was no involvement of the ribs, and the tumor mass appeared to be anterior to them. No roentgenographic diagnosis was possible.

First Operation.—Nov. 28, 1922: The tumor was exposed by a transverse incision just below the clavicle. It proved to be cartilaginous, 6 cm. in diameter, lying between the first and second ribs, extending inward to the pleura and outward between the ribs for 2 cm. There was erosion of the first rib. The tumor was excised down to the ribs and then curetted out as far as seemed safe without penetrating the pleura. One hundred milligrams of radium screened with 2 mm. of brass was left in the cavity for twelve hours.

1. Hedblom: Tumors of the Bony Wall of the Chest. *Ann. Surg.* 35:5 (July) 1921.



Fig. 3 (case 1).—Lateral view of tumor.



Fig. 2 (case 1).—Recurrence of tumor at original site. The area is less dense.



Fig. 5 (case 1).—View of tumor showing denser shadow but without apparent extension.



Fig. 4 (case 1).—Greatly increased area of density extending outward to lateral border of the chest.

Second Operation.—July 21, 1924: The old scar was excised and the incision enlarged. The tumor had recurred at the original site. The first rib was eroded and destroyed for 2 or 3 cm. outward from its sternal junction. There were two or three recurrent nodules in the periosteum overlying the second rib. The second rib was removed for 2 inches (5 cm.), the first rib and sternum thoroughly curetted. The pleura was accidentally opened but no serious symptoms followed. Fifty milligrams of radium in bare needles were inserted into the area of the tumor. The radium was left in ten hours. The patient remained well until May 20, 1927, when she returned complaining of pain in the right arm and some restriction of motion. The tumor had recurred in the scar in the second rib farther out and beneath the clavicle. X-ray examination showed involvement of the second, third and fourth ribs.

Third Operation.—June 13, 1927: A large flap was made by a curved incision beneath the breast and pectoral muscles. The second, third and fourth ribs were



Fig. 7 (case 1).—Scar from operation; the right breast is slightly elevated.

divided at the sternocostal junction and the pleura opened to inspect the tumor. It had involved the third rib in the anterior axillary line and there was an extension within the chest cavity involving the second, third and fourth ribs and the parietal pleura. A tumor mass 5 or 6 inches (12.7 or 15.24 cm.) in diameter projected into the pleural cavity and was attached to the upper lobe of the lung. The tumor masses involving the ribs were all curetted and 50 mg. of radium in 12.5 mg. bare needles was inserted into the tumor mass within the chest cavity and left in twenty-four hours. The defect in the wall of the chest was closed by sliding up the breast and pectoral muscles. The wound healed without infection.

Present Condition.—Feb. 10, 1928: Clinically, this patient has remained well, but a recent examination revealed a tumor mass 2 cm. in diameter between the axillary folds, firmly attached to the wall of the chest. X-ray films do not show any increase in the size of the tumor within the chest cavity.

Pathologic Process.—Grossly, this tumor consisted of pearl-like cysts which formed pockets in the cartilage of the ribs and later invaded the bony portions of the ribs and manubrium.



Fig. 6 (case 1).—Lateral view of tumor showing invasion of pleura and lung.

The microscopic report was made by Dr. A. M. Moody. The tissue consisted essentially of hyaline cartilage with many nuclei, having the appearance of dividing cells and some round cells. As a whole, it presented the picture of a malignant growth. A diagnosis of chondrosarcoma was made (figs. 1 to 8).

CASE 2.—A man, aged 26, a concrete worker, for one month prior to my first examination had noticed a swelling in the region of the right pectoral muscle just below the clavicle. Six years before, he was struck on the chest with a piece of iron, near the site of the present tumor. The scar of this injury is still visible. He was otherwise healthy. The results of the examination were negative except for the presence of a semifluctuating tumor, 6 cm. in diameter lying just beneath the right clavicle and extending from the outer border of the sternum to a line drawn from the central portion of the clavicle. The tumor was painless, some-

DATA IN CASE 2

200 Kilovolts, 4 Milliamperes, 50 Cm. Distance, 18 Cm. Aperture, $\frac{1}{2}$ Mm. Copper,
1 Mm. Aluminum Filter

| | | |
|----------|---|------------|
| 12/15/26 | Upper anterior right side of chest..... | 15 minutes |
| 12/16/26 | Upper anterior right side of chest..... | 15 minutes |
| 12/17/26 | Upper anterior right side of chest..... | 20 minutes |
| 12/20/26 | Upper anterior right side of chest..... | 20 minutes |
| 12/22/26 | Upper anterior right side of chest..... | 20 minutes |
| 12/24/26 | Upper anterior right side of chest..... | 20 minutes |
| 12/27/26 | Upper anterior right side of chest..... | 10 minutes |
| 12/27/26 | Right posterior angle of scapula..... | 10 minutes |
| 12/29/26 | Right posterior angle of scapula..... | 20 minutes |
| 1/ 3/27 | Right posterior angle of scapula..... | 20 minutes |
| 1/ 5/27 | Right posterior angle of scapula..... | 20 minutes |
| 1/ 8/27 | Right posterior angle of scapula..... | 30 minutes |
| 1/10/27 | Right posterior angle of scapula..... | 20 minutes |

Pain diminished; mass in back became smaller; open wound in anterior aspect of chest cleaner

| | | |
|---------|------------------------------------|------------|
| 2/ 8/27 | Right anterior side of chest..... | 30 minutes |
| 2/ 9/27 | Right anterior side of chest..... | 30 minutes |
| 2/11/27 | Right anterior side of chest..... | 30 minutes |
| 2/12/27 | Right posterior side of chest..... | 30 minutes |
| 2/18/27 | Right posterior side of chest..... | 30 minutes |

Following first treatments pain ceased; general condition improved; wound in anterior chest wall closed in considerably; remaining area shows clean granulations.

what movable and apparently attached to the underlying structures. X-ray films revealed an area of only slightly increased density at the site of the tumor.

Operation.—July 29, 1926: A curved incision over the wall of the chest exposed a tumor, 6 cm. in its long diameter, densely adherent to the third rib and involving its periosteum. The tumor was vascular and had infiltrated the pectoral muscles and passed between the third and fourth ribs, involving the parietal pleura. The tumor was excised as widely as possible; 50 mg. of radium screened with 2 mm. of brass was left in the wound for twelve hours. The wound did not heal readily. There was a free discharge of cheesy material and free hemorrhage. In September, 1926, 50 mg. of radium was placed in the cavity in bare needles for two hours. The wound improved much after this and granulations assumed a healthy appearance, but a pocket still persisted which continued to discharge and bleed.

Nov. 8, 1926: Four months after operation, 1,200 mg. hours of radium in bare needles were given in different portions of the tumor. There was a well marked constitutional reaction and the tumor shrank greatly. However, it continued to bleed freely and at each dressing fragments of grayish necrotic material escaped. At this time, a tumor appeared near the angle of the right scapula

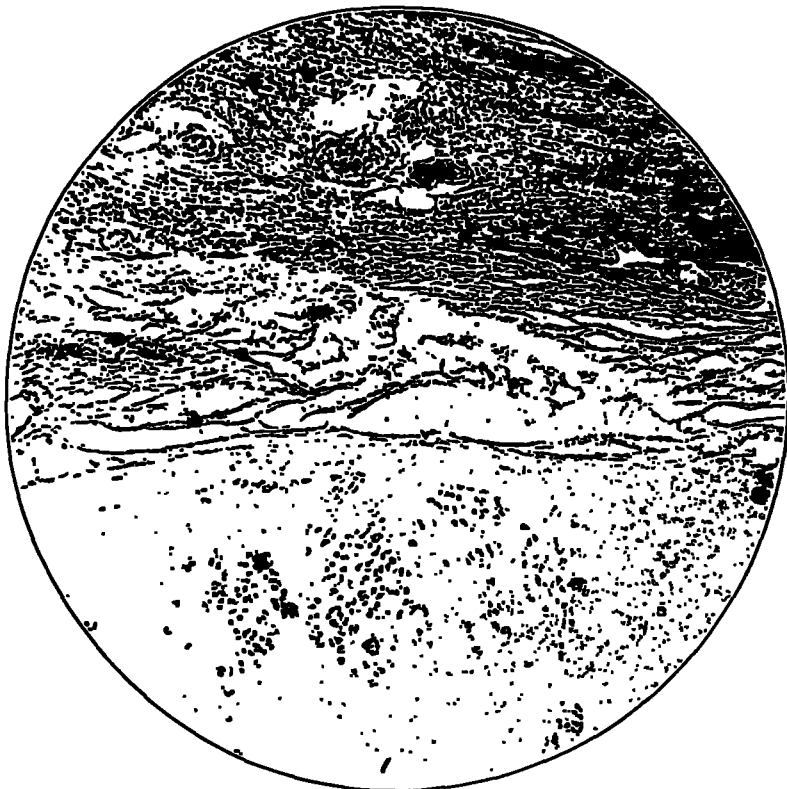


Fig. 8 (case 1).—Tumor of the wall of the chest; chondrosarcoma; $\times 75$

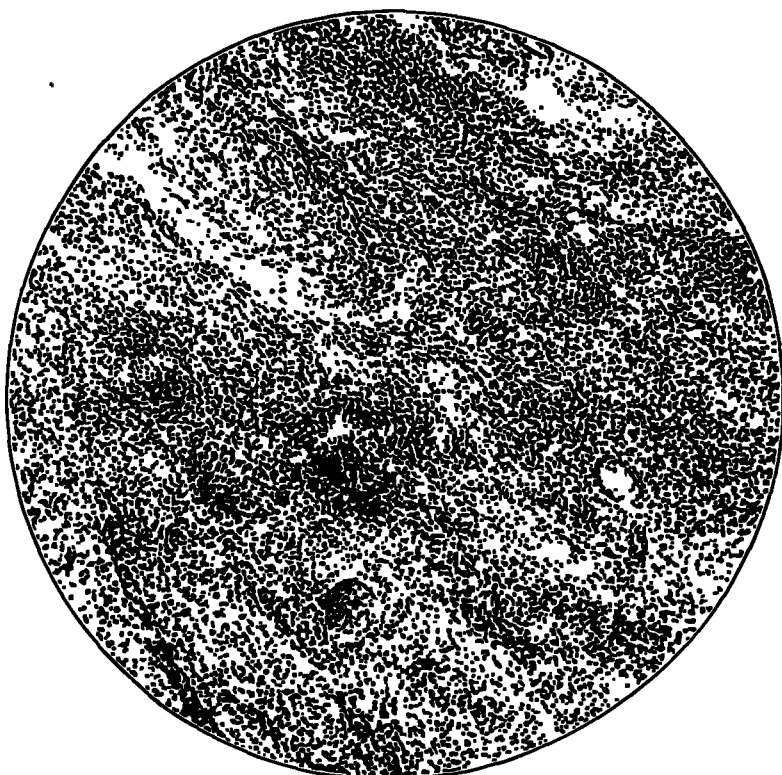


Fig. 9 (case 2).—Tumor of the wall of the chest; round cell sarcoma; $\times 75$.



Fig. 12 (case 2).—Sarcoma of the wall of the chest.



Fig. 13 (case 2).—Metastatic sarcoma of the back.

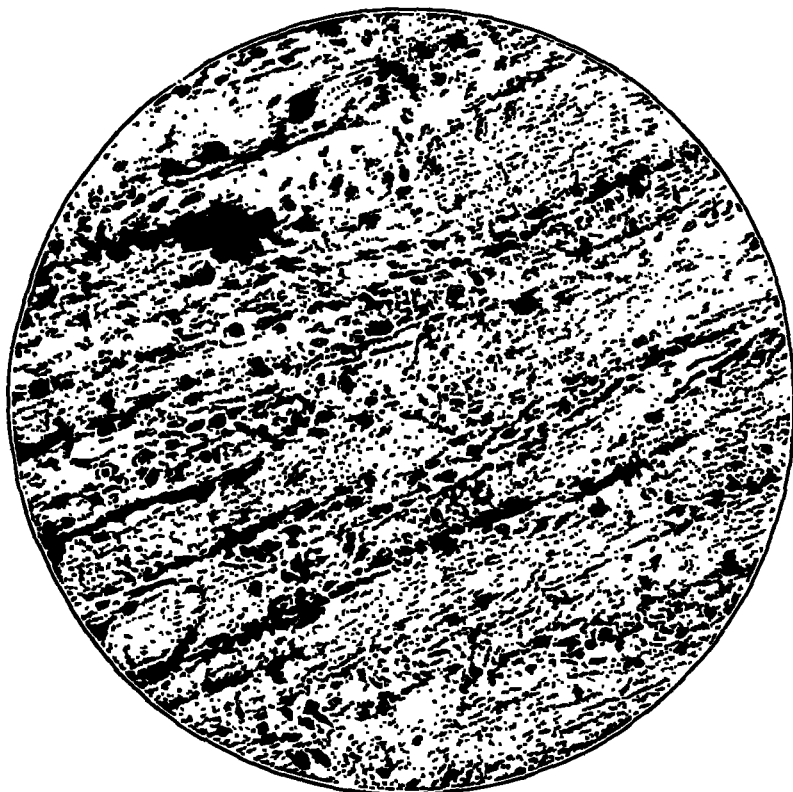


Fig. 10 (case 2).—Same as figure 9, showing more detailed structure; $\times 300$.



Fig. 11 (case 2).—Infiltration of the muscle fibers; $\times 100$.

CRANIOTOMY INCISIONS WITHOUT FORCEPS*

ALBERT S. CRAWFORD, M.D.

DETROIT

The control of hemorrhage is one of the most important and yet difficult problems in all extensive craniotomies. The tourniquet, hemostatic stitch and pedicle clamp have been replaced largely by the multiple forceps method now commonly used. The covering of the scalp is generally accomplished by towels clamped or sewed to the cut edges.

During the past two years, my co-workers and I have been using a method which keeps the operative field free of forceps and which at the same time efficiently covers the scalp, controls bleeding and protects the edges of the incision. This is by the use of stockinet and Michel clips.

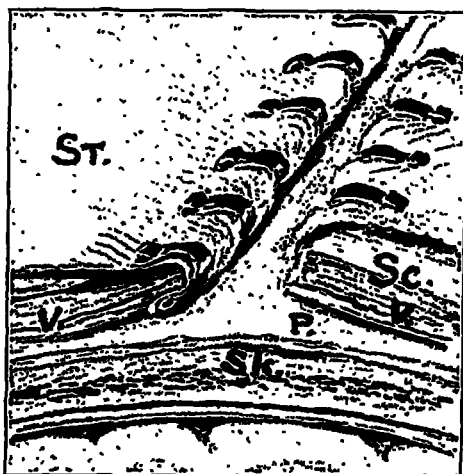


Fig. 1.—Placement of Michel clips on skin incisions. *ST*, indicates the stockinet covering; *Sc*, the scalp; *V*, the vein; *P*, the pericranial layer and *Sk*, the skull.

We experimented on various metal clips, but finally settled on the Michel type, for they are already available, are inexpensive, are easily applied and control hemorrhage efficiently.

A few points in the technic might be mentioned. After the field block has been made with procaine hydrochloride, the incision line is scratched till it bleeds, then the stockinet is laid over the whole operative field and cut along the blood-stained line. The skin incision is made in the usual manner, a few inches at a time, and bleeding is controlled by digital pressure. When a spurting vessel is encountered, it is caught at once and stick tied with silk. All other oozing is controlled with the clips. Figure 1 shows how the clips are placed, external to the

*From the Henry Ford Hospital.

which was similar in appearance and consistency to the original tumor. The patient was now referred to the x-ray department for deep therapy. He was given treatments to the point of tolerance. He had a severe reaction from the x-ray therapy. There was marked improvement in the original tumor with diminished discharge and less hemorrhage. The tumor on the back almost disappeared.

Pathologic Process.—Grossly, this tumor consisted of grayish white tissue. It was soft, friable and seemed to infiltrate the muscle. There was no regular form or contour. In places, it seemed glandular (fig. 9 to 13).

Microscopically, it consisted of small round cells, infiltrating the adjacent muscle fibers. A diagnosis of round cell sarcoma was made.

Present Condition.—Feb. 10, 1928: The patient has lost 10 pounds (4.5 Kg.) in weight; he is anemic and weak. The tumor has not increased in size but it is still discharging, bleeds freely and has eroded the second rib. There is a dense fibrosis of the pectoral muscles, and he is unable to abduct his arm or lift it above his head. The tumor over the scapula has not recurred, but there is an ulcer 2 cm. in diameter at its former site. No metastasis can be discovered either by examination or on the x-ray films.

COMMENT

Tumors of the wall of the chest are usually malignant. The most common forms are sarcoma and chondrosarcoma. These tumors usually recur after removal. The patients are best treated by thorough removal, radium and x-ray therapy.

Unfavorable results have not followed this method so far. Some sloughing of the skin edges occurred in one case, resulting in delayed union, but this was attributed to extremely low blood pressure following the operation and to probable thrombosis of the vessels. The clips, of course, may have been contributing factors. This danger from pressure should be kept in mind.

Essentially the same method was recently described for incisions on the extremities by Dr. W. E. Johnston.¹ We agree with him that the method can be effectively used for protection of wounds in all surgical incisions, except probably those leading to large cavities, such as in laparotomies, in which clips might be dislodged and lost. A refinement in technic might be elaborated by having the clips all fastened to a string or wire, which would eliminate the danger of any being lost.

1. Johnston, W. E.: Method of Operative Protection from Skin Infection, *J. A. M. A.* **88**:1320 (April 23) 1927.

pericranial layer, about 12 mm. apart and directly over bleeding points wherever possible. Figure 2 shows a temporoparietal incision all ready for the work on the skull, and figure 3 the clips, the holder and the forceps used.



Fig. 2.—Temporoparietal incision with clips already placed.

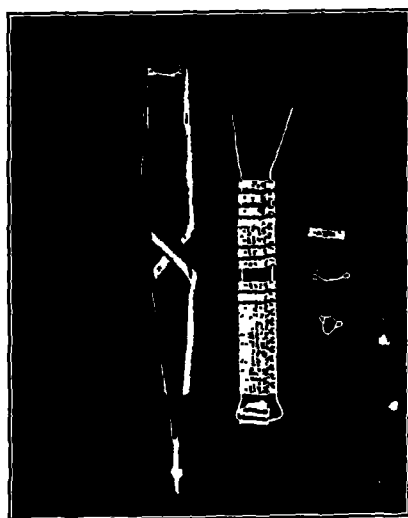


Fig. 3.—Michel clips (small size) single (top and side views), on the wire holder, and one in the forceps which is used to apply (reduced one-half).

After the bone flap has been turned, the wound edges are covered with wet cottonoid sheets, so that the field is smooth and level and the clips are protected. During closure, the clips are removed a few at a time, as the skin sutures are placed and tied, to prevent excessive bleeding from the scalp.

sciousness and an x-ray picture is made, it is found, however, that the reestablished muscle spasm has again pulled the fragments out of alinement. The remedy is manifestly to be found in traction or extension to avail of not only marshaling the fragments by the encircling soft parts, but to overcome muscle spasm before final fixation. In such cases, the traction should be continued until the muscle spasm ceases. Fractures at the middle of the forearm, after reduction with immediate fixation, are most prone to get out of alinement from the continuance of muscle spasm of the pronators, with an ultimate lessening of the interosseous space and rotatory movements of the forearm, unless corrected early.

Economy in x-ray pictures, after reduction of fractures and prior to good callus formation, is false economy, and the relation of the fragments to each other should be frequently determined, not presupposed, especially in the early stages of healing.

In order to emphasize the points that I desire to bring out in this paper, it may be well to recapitulate certain points concerning aids in restitution which should be considered.

1. Traction on the surrounding encircling soft parts should be utilized to help assemble the fragments, in addition to any manipulation or leverage that the surgeon can effect from without.

2. The possibility of postanesthetic muscle spasm pulling the fragments out of alinement must be borne in mind. In suitable cases, it will be well to use traction until muscle spasm is permanently overcome.

3. Fixation should be used only after muscle spasm is overcome in cases in which muscle spasm can distort the parts.

4. X-ray pictures should frequently be made until callus formation assures the desired restoration. The surgeon should not be content with an x-ray picture before the cast or splint is applied and after it is taken off.

REPORT OF A CASE

In order to illustrate the foregoing principles, the following case will be cited as being typical.

H. C., aged 28, fell off a platform about 8 feet high (244 cm.) on June 27, 1926, striking on his left shoulder. A report of his condition at that time states that pain and crepitation were present. A depression was noted under the left acromion process, and there was undue fulness on the anterior aspect of the joint. The arm was rotated inward and abducted, and the forearm was supported by the right hand, near the elbow.

An x-ray picture made at that time showed a fracture dislocation at the proximal end of the left humerus. The dislocation was of the subcoracoid type, being anterior and inward from its proper position, so that the glenoid was not visible in the roentgenogram. The fracture was of the surgical neck, and from the

FRACTURE DISLOCATION OF THE SHOULDER

RELATION OF SOFT PARTS TO RESTORATION: A NEW METHOD OF TREATMENT

R. TUNSTALL TAYLOR, M.D.

Professor of Orthopedic Surgery, University of Maryland

BALTIMORE

As a general rule, a fracture or dislocation is thought of by the general practitioner solely in terms of the relation that bones or fragments of bones bear to each other. The effect of the soft parts in restoring normal alinement or in preventing it is lost sight of.

The interposition of soft parts in preventing union, causing malunion or interfering with restitution is well recognized and will not be discussed. But the clinician with increasing experience is more and more impressed with the importance of the utilization of the closely encircling muscles, ligaments, tendons, capsule and periosteum or portions of the latter in marshaling fragments into alinement. Failure to consider this important factor often leads to poor end-results, disappointment to the attendant or serious disability to the patient.

In such complicated joints as those of the shoulders and hips, this is especially important, and a precise knowledge of the anatomy of the parts, the exact function of each muscle and the direction of the forces that produced the disability should be known.

In the treatment of patients with intracapsular fracture of the hip, Royal Whitman of New York places the patient in the now well recognized "Whitman position," and by extreme abduction makes use of the capsule put on the stretch to marshal the fragments into apposition. This is aided through fixation of the pelvis by abduction of the other leg and by traction and inward rotation of the affected one. In this connection, Lovett and Jones¹ say that "any treatment which ignores the fundamental principles of abduction, extension and internal rotation in intracapsular fracture of the hip, should be ruthlessly condemned as obsolete," but they fail to explain the *modus operandi* of the soft parts.

During the early stages of fractures and dislocations, muscle spasm is known to play an important rôle in preventing reposition, but its continuance after reduction is frequently overlooked. Thus, with the patient under an anesthetic, a fracture is reduced and the part involved placed in a carefully applied plaster cast, and the surgeon has a comfortable feeling that all is well. When the patient regains con-

1. Lovett and Jones: *Orthopaedic Surgery*, New York, William Wood & Company, 1923, p. 404.



Fig. 2.—Fracture-dislocation in plaster cast after attempt at manipulative reduction.

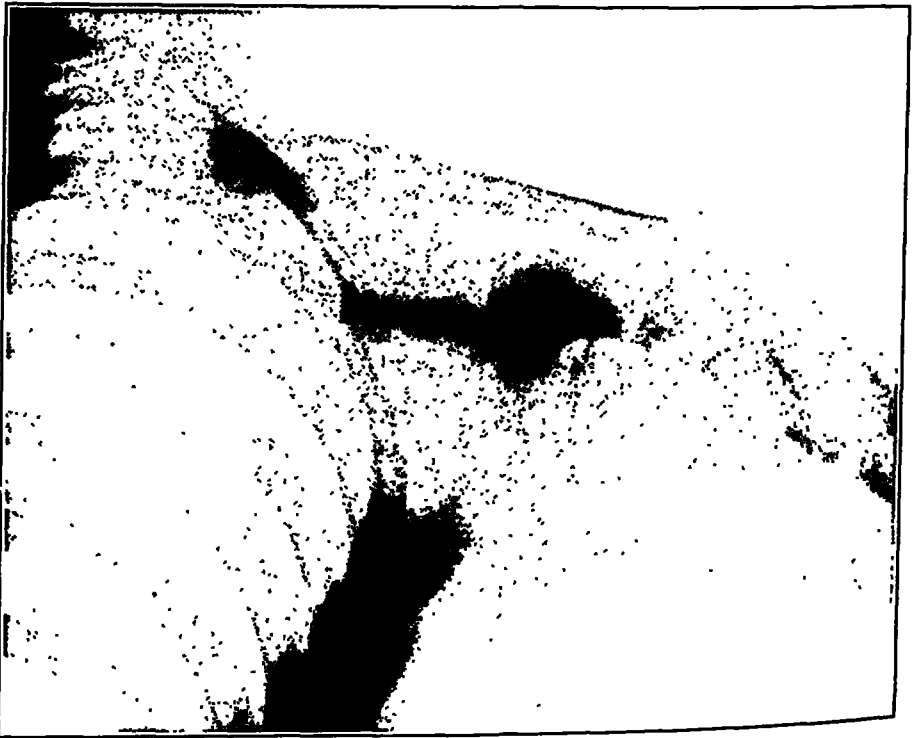


Fig. 3.—Forty-eight hours after traction (15 pounds) on distal fragment and suspension of 5 pounds each of the forearm and humerus to separate pulleys. Abduction of humerus 60 degrees. Dislocation reduced.

muscle spasm of the supraspinati and infraspinati the proximal fragment or humeral head had rotated through an arc of 180 degrees, so that its fractured surface was directed upward; the line of fracture of the distal end was horizontal and slightly below and external to the articular surface of the fractured humeral head (fig. 1).

Prior to the time the patient entered my service, an attempt had been made to reduce the fracture and dislocation while he was under an anesthetic, with the result that the distal fragment had slipped into the axilla and was abducted at an angle of 45 degrees with the body and was causing much axillary pain from impingement on nerves. The proximal end or head was unchanged in position. After this manipulation, it was held in position by a plaster cast covering the arm



Fig. 1.—Fracture-dislocation of left shoulder immediately after accident.

and thorax (fig. 2). The patient was referred to me in this condition seven days after the accident, and was admitted to the hospital on July 2, 1926.

For this condition, various manipulative procedures of doubtful value have been suggested and tried, with the patient under general anesthesia; also similarly ineffective open-operative methods of grafting, suture, screwing the parts together, bone-pegging and even removal of the dislocated proximal fractured head. In these cases, it is wisest to put into practice the principles set forth in the first part of this paper. As in the present case neither the dislocation nor the fracture had been reduced by manipulation, the retaining cast was removed and the patient put up in a Balkan frame. He was placed flat on his back with the spring and mattress made additionally firm by cross-slats. Projecting from under the mattress beyond the left side of the bed for about 2 or 3 feet (61 or 91 cm.) was a board 5 feet (152 cm.) long and 4 inches (10 cm.) wide; to its upper surface at the

sion of the forearm and of the arm, and in abduction at the side of the bed, from 10 to 15 pounds (4.5 to 6.8 Kg.) were used as the case progressed (figs. 3 and 4).

This apparatus was applied on July 2, and on July 6, the x-ray picture showed that reduction of the dislocation had been effected (fig. 5). Abduction of the arm at this time was about 45 degrees with the body, and it was seen that the apposition of the fragments was not in good alinement. It was therefore increased to 60 degrees and later to 90 and 120 degrees until perfect alinement was obtained (figs. 5, 6 and 7).

On July 28, after three weeks of treatment in bed, when the x-ray examinations showed good callus and a reduction of the dislocation and normal alinement at the fracture, the arm was carefully held in the position maintained by the



Fig. 6.—Abduction of humerus 90 degrees.

Balkan frame apparatus, the patient slowly assisted into a sitting position in the bed, and a plaster cast applied from the left hand to below the crests of the ilia (fig. 8).

This position was approximately with the humerus abducted 120 degrees with the body, rotated outward 60 degrees and the forearm flexed 90 degrees.

The cast was bivalved horizontally on August 19, so that the upper portion could be removed to permit massage and passive upward and anteroposterior motions. On September 2, the cast was removed, a cravat sling used and passive and active motions permitted to allow full function, which soon followed.

In approximately ten weeks following a fracture dislocation, this man was back on the job with full restoration of function.

The method used has proved satisfactory in this and similar cases. It substantiates the claim made that the soft parts may aid materially

outer end a similar piece of board, about 4 by 4 inches was nailed at right angles; at its center it was surmounted by a vertical pulley, which was screwed in. By means of this rough board, which the mattress and the patient's weight held in any position in which it might be placed by the surgeon, horizontal traction over the pulley could be made at any desired angle of abduction by means



Fig. 4.—Position of patient in Balkan frame.

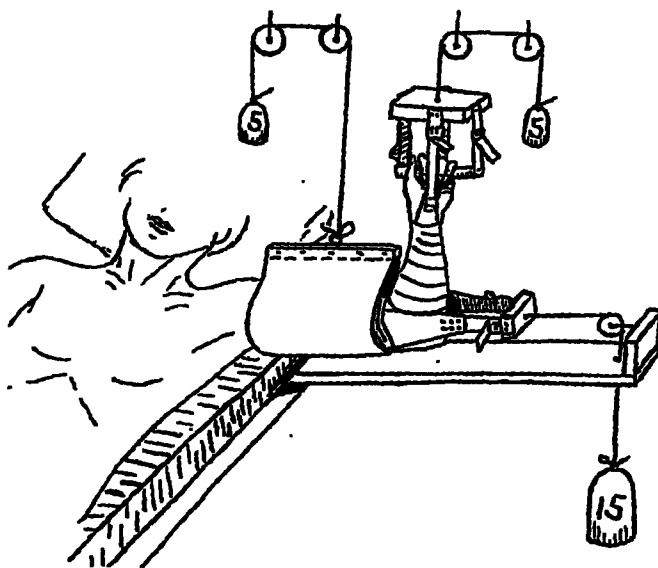


Fig. 5.—Diagrammatic drawing of apparatus.

of adhesive straps and a spreader attached to the upper arm. The forearm, by means of adhesive traction straps from elbow to hand, and the upperarm, supported by a sling with spreader, were suspended from the overhead bars of the Balkan frame, with appropriate pulleys and counter-balance weights. These enabled the patient to change his position within reasonable limits and facilitated nursing. About 5 pounds (2.3 Kg.) each were used as counterpoises for suspen-

in reducing dislocation and getting the parts of fractures in line when by properly directed traction muscle spasm is overcome.

I claim, therefore, that traction in abduction and outward rotation, putting the capsule on the stretch, in early treatment will reduce anterior and inward dislocation of the humeral head and that hyperabduction, carefully guided by a series of x-ray studies, may entirely overcome the nonalignment in this most disabling condition.

In contrast, it may be well to review briefly comments in leading textbooks on the prognosis and treatment of this serious injury.

C. L. Scudder,² speaking of fractures, epiphyseal separations and dislocations of the humeral head, says:

"An anaesthetic must be used for examination and diagnosis, but it is even more important, however, that the first retentive dressing be applied with the assistance of an anaesthetic. Traction, counter traction and manipulation will secure coaptation of the fragments. To hold these fragments securely is difficult—to hold any one of these fractures without operative interference may be impossible." He recommends after reduction, a V-shaped axillary pad, coaptation splints, a plaster shoulder-cap and arm and body plaster of paris or crinoline, with arm at the side and forearm across abdomen, thus rotating the lower fragment inward, the malposition of fracture in this region. Further on, he says that "if traction on the humerus and pressure on the loose head in the axilla fails, open incision is to be done, using the McBurney-Porter hook on the upper fragment and if successful, suturing the shaft with absorbable suture or fine silver wire. . . . If it is impossible to reduce the dislocated head or if it is much comminuted, it will be necessary to excise it."

Sir Robert Jones³ says:

"The upper fragment formed by the articular head is liable to be rotated into any position and dislocated from the glenoid surface . . . A rotated or dislocated intra-articular fragment will very probably require reposition by operation; this is easily done by the anterior deltoid incision, but there is some liability to recurrence of displacement. If this recurrent displacement cannot be prevented by one or two screws driven through the tuberosity, the head of the bone ought to be removed, but resection more extensive than this is to be avoided."

He also recommends the axillary pad to prevent the adduction of the upper end of the lower fragment, and in closed reductions, he straps the inward rotated arm to the body.

2. Scudder, C. L.: *Treatment of Fractures*, ed. 3, Philadelphia, W. B. Saunders Company.

3. Jones, Robert: *Orthopaedic Surgery of Injuries*, London, Oxford University Press, 1921.

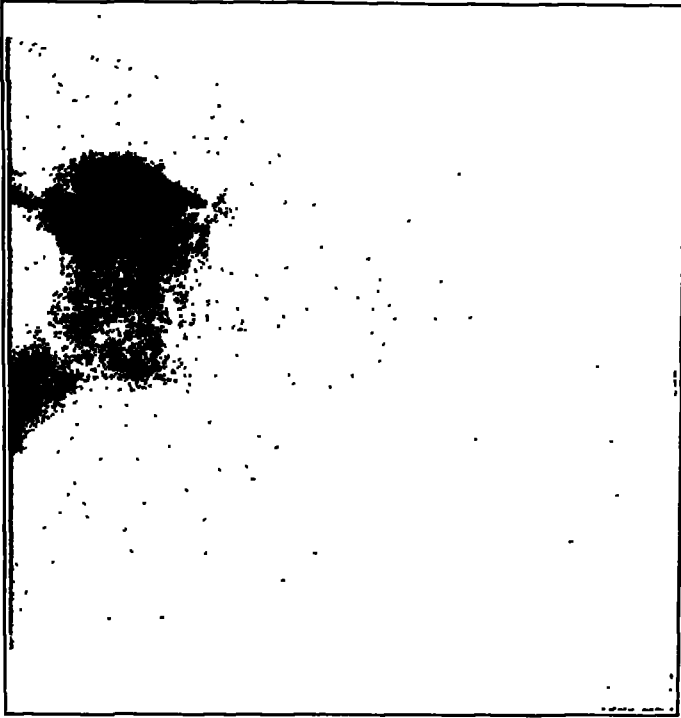


Fig. 7.—Abduction of humerus about 120 degrees. Fracture reduced and perfect alinement. Note intact periosteum between fragments seen below.



Fig. 8.—Patient shown in plaster cast shortly after application in same position as that maintained in the Balkan frame.

WOUNDS OF THE HEART

REPORT OF TWO CASES *

D. M. COX, M.D.

LOUISVILLE, KY.

Of penetrating wounds of the thorax, those involving the heart are relatively infrequent. During the past four years, there have been thirty-five cases of gunshot wounds and sixty-one of stab wounds of the chest at the Louisville City Hospital. Only one bullet and one knife encountered the heart; some of the other wounds were very near, striking the pericardium, but none of the patients gave symptoms to warrant operative intervention.

Early history contains records of many cases of injuries to the heart, and in each instance the patient died. Aristotle and Galen believed that heart wounds were always fatal. Hollerius¹ (1498-1562) was the first to oppose this idea; he thought that small wounds which did not bleed excessively could heal. The first authentic record of a healed wound of the heart was by Iodinis Wolf² in 1642. He found a scar in the heart of a deer, and believed that the animal had received the wound previously and had recovered. In 1761, Morgagni³ was of the opinion that a rapid collection of blood in the pericardial cavity could compress the heart and stop its action.

In 1868, Georg Fischer⁴ collected from the literature a series of 452 cases of wounds of the heart with a mortality of 90 per cent. The treatment employed at that time was rest, venesection, application of leaches and occasionally, when possible, the passage of a catheter or sound into the wound for evacuation of fluid from the pericardial cavity.

In 1881, Roberts⁵ suggested that wounds of the heart might be sutured. Suture of the heart muscle was first performed experimentally on rabbits by Black⁶ in 1882. The idea met with much opposition—

*From the Department of Surgery, University of Louisville School of Medicine.

1. Hollerius, J.: *Communis aphorismi allegati*, quoted from Beck: *Wounds of the Heart*, Arch. Surg. 13:205 (Aug.) 1926.

2. Wolf, Idonis, quoted from Beck.

3. Morgagni, J. B.: *De Sedibus et Causis Morborum*, Lipsiae, sumptibus Leopoldi Vossii, 1829; quoted from Beck.

4. Fischer, Georg: *Die Wunden des Herzens und des Herzbeutels*, Arch. f. klin. Chir. 9:571, 1868; quoted from Beck.

5. Roberts, J. B.: *The Surgery of the Pericardium*, Am. Anat. & Surg. 4: 247, 1881.

6. Black: *Verhandlungen der deutschen Gesellschaft für Chirurgie*, Elften Congress, Berlin, 1882, part 1, p. 108; quoted from Beck.

According to Jones and Lovett:⁴

"This accident (fracture-dislocation) is very crippling and if all trials at reduction fail, an open operation should be performed and the head reduced, an ivory or bone peg being used, if it is found necessary." The Jones rectangular arm splint is then described. Later they say: "If the fracture is at the surgical neck and the head is dislocated, an open reduction should be effected and a plate or graft used After all operations for reducing fracture and fracture-dislocation about the shoulder, except for fractures in or near the glenoid cavity, the arm should be kept in the abducted plane." This does not coincide with Jones' recommendation of closed reduction.

F. J. Cotton⁵ says:

"Fracture of the surgical neck complicating dislocation does occur and is a most formidable complication Obviously all our methods of reduction are of little use in this condition; it is possible that enough connection of fragments may be retained to permit of reduction by right angled traction with outward pressure on the head. If such attempt at reduction does not succeed, as it usually does not, there is nothing for it but to operate."

CONCLUSIONS

The temptation is great to avail oneself of the open operative treatment for fractures whereby one can see exactly what is the situation inside and act accordingly.

Here, however, is a condition wherein utilization of the soft parts and not cutting or further traumatization is indicated. They should be used as tractors to overcome dislocation, muscle spasm and non-alinement of fragments at the shoulder joint.

On account of some of the mutilated and impaired functional results seen after manipulative and operative treatment of fracture dislocation of the shoulder, I feel that the method herein advocated should and can be standardized. Further, probably with the exception of the aid of the x-ray, it can be applied in rural communities far away from great medical centers and hospitals.

207-208 Medical Arts Building.

4. Jones and Lovett: *Orthopaedic Surgery*, New York, William Wood & Co., 1923, p. 413.

5. Cotton, F. J.: *Dislocations and Joint Fractures*, Philadelphia, W. B. Saunders Company, 1924, p. 211.

heart and may be used without entering either pleural cavity; however, in most injuries the pleural cavity has already been penetrated.

After the heart has been exposed, there are several methods by which the wound may be found and repaired: 1. The heart may be grasped tightly and forcibly pulled out of the wound, where gradual relaxation will reveal the injury, which can then be sutured. 2. The first impulse would be to plug the bleeding area with the finger. This is difficult to carry out, because the beating organ keeps moving out of the way of the finger. If sufficient pressure is exerted to control the bleeding, the friable muscle is apt to be torn and increase the size of the wound. 3. In 1907, Sauerbruch¹⁰ described a method by which the bleeding could be controlled: The middle finger of the left hand is inserted through the great transverse sinus which is situated below the aorta and pulmonary arteries and above all the veins entering the heart. The fourth and fifth fingers are placed below the veins; the latter can be compressed by bringing the third and fourth fingers closer together, and thus keep all blood from entering the heart. The index finger and thumb are left free to steady the heart while the wound is sutured. This pressure cannot be maintained indefinitely, for the heart tolerates ischemia for only a limited period of time. This period of safety has been worked out on animals and varies from $1\frac{1}{2}$ minutes⁸ in the dog to $3\frac{3}{4}$ minutes¹¹ in the rabbit. To prolong the ischemia beyond this period of time causes the heart to lose its normal rhythm, which it never regains, or there is subsequent degeneration of the cortical cells. 4. A much simpler procedure was recently developed by Beck and Cutler¹² in doing some experimental work on a method for the surgical relief of mitral stenosis. This method will be given in detail in the first case report.

REPORT OF CASES

CASE 1.—M. P., aged 26 (?), was admitted to Louisville City Hospital at 11 a. m. on Oct. 14, 1926. He had received a gunshot wound in the chest a few minutes before admission, the bullet entering just to the left of the sternum in the fifth intercostal space. There was pain only at the site of injury. Examination did not reveal any pathologic process of the lungs; the heart was normal in size, but the sounds were faint; the pulse was weak, with a rate of 84.

Fluoroscopy was performed. The field of the right lung was slightly hazier than that of the left, but there was no conclusive evidence of fluid or pneumo-

10. Sauerbruch, F.: Die Verwendbarkeit des Unterdruckverfahrens bei der Herzchirurgie, *Arch. f. klin. Chir.* 83:537, 1907; quoted from Beck.

11. Laewen, A., and Sievers, R.: Experimentelle untersuchungen über die chirurgisch wichtigen Abklemmungen des grossen gefäße in der Nähe des Herzens unter besonderer Berücksichtigung des Verhältnisse bei der Lungen embolie operation nach Trendelenberg, *Deutsche Ztschr. f. Chir.* 94:5, 1908; quoted from Beck.

12. Beck, C. S., and Cutler, E. C.: A Cardiovalvulotome, *J. Exper. Med.* 40: 375 (Sept.) 1924.

many prominent surgeons spoke discouragingly concerning the subject. Del Vecchio⁷ experimentally incised the hearts of dogs, then sutured the wounds, and the animals recovered. In 1895, he demonstrated these healed wounds to the Eleventh International Medical Congress in Rome, Italy. During the following year, three human hearts were sutured; the first two patients died following the operation, while the third (operated by Rehm⁸) lived and returned to normal life.

In 1920, Tuffier⁹ collected 305 cases of sutured wounds of the heart, in 50.4 per cent of which the patients recovered. This probably is a rather high percentage because surgeons are more prone to report their successful cases.

The prognosis depends on the type and extent of the injury. Wounds which penetrate into the cardiac cavity and leave an opening in the heart wall sufficiently large for the escape of much blood are usually fatal in a short time. The clinical picture of the less extensive wounds depend largely on the size of the opening in the pericardium. If there is a fairly large opening providing free escape of blood, the symptoms produced are those of any severe hemorrhage. If the pericardial rent is small and blood collects in the pericardial cavity, compression of the heart results; the arterial pressure is lowered, and the venous pressure is elevated. When the intrapericardial pressure becomes equal to the venous pressure, the heart ceases to function; this condition is called heart tamponade. During the process of compression (or tamponade) cyanosis develops, the pulse grows weaker and more rapid, heart sounds become distant, and respiration is increased.

A surgeon may be called to meet a cardiac emergency at any time; therefore, he should be familiar with the various methods of operative technic, and know how they can best be applied under different conditions. The earlier operations were performed through an opening obtained by the removal of one rib. This, however, gave poor exposure. Later methods include: (1) removal of two or more ribs and costal cartilages subperiosteally; (2) hinged flaps consisting of skin, muscles, ribs and possibly a portion of the sternum; (3) median sternotomy; (4) intercostochondral thoracotomy—that is, two, three, or four costal cartilages are divided near the sternum and the ribs retracted until sufficient exposure is obtained. The last two methods are probably the most satisfactory. Median sternotomy gives the best exposure of the

7. Del Vecchio, S.: *Sutura del Cuore*, *Riforma med.* **11**:38, 1895; quoted from Beck.

8. Rehm, L.: *Ueber penetrierende Herzwunden und Herznaht*, *Arch. f. klin. Chir.* **55**:315, 1897; quoted from Beck.

9. Tuffier, T.: *La chirurgie du coeur*, Cinquieme congrès de la Société Internationale de Chirurgie, Paris, July 19-23, 1920; *Extrait*, Brussels, Haye, 1920; quoted from Beck.

anesthetic being used. The edges of the wound were retracted, and the pulsating heart was seen in a pool of blood.

A suture was placed in the apex of the heart; this was used for traction by holding it in the left hand, while the left index finger examined the heart carefully. There was a longitudinal incision 3 cm. long in the anterior portion of the right ventricular wall, extending to a depth of about 6 mm. Owing to the length of the wound, hemostatic sutures were not used. The index finger held over the wound controlled the bleeding, while interrupted silk sutures were applied to approximate and close the edges of the wound. When this was accomplished bleeding ceased. All the blood was then cleared out of the pericardial cavity; this afforded an excellent view of the wound, which was about 5 mm. from the coronary artery. None of the sutures had pierced or included that structure. The pericardium was closed with interrupted silk sutures, which did not make an air-tight pericardial cavity. There were three openings (each about 15 mm. in diameter) in the left pleural cavity; these were not closed. The wall of the chest was closed air tight. A needle was inserted into the left pleural cavity and about 1,500 cc. of air removed, thus relieving the pneumothorax.

During the first thirty-six hours after the operation the temperature was between 99 and 100 F., the pulse rate between 100 and 126, and the respiration from 58 to 70. The patient's breathing was shallow, and there was some air hunger. He was thirsty, took fluids well, and retained them. His temperature then rose and for four days remained between 101 and 102.4 F. The heart rate averaged around 130 and went up as high as 152. The respiration gradually went down to around 40. Nourishing foods were given, he was digitalized and treatment with small doses of digitalis continued.

July 19: Examination showed pneumonia of the base of the left lung. Pericardial effusion and dulness (extending 6 mm. to the right of the midline) were present, and a pericardial friction rub was heard.

July 22: The left border of the area of cardiac dulness extended to the anterior axillary line and the right border 10 cm. to the right of the midline. There was evidence of fluid in the left pleural cavity at that time. Slight separation of the edges of the wound, with the drainage of a small amount of pus, was noted.

July 24: The pericardial cavity was aspirated through the fourth interspace just to the right of the sternum, and 110 cc. of straw-colored fluid was obtained. The left pleural cavity was aspirated, and only 50 cc. of bloody fluid was obtained. *Staphylococcus aureus* was cultured from the pericardial fluid and from the pus of the wound. The pleural fluid was sterile.

July 26: Two hundred cubic centimeters of fluid was aspirated from the pericardial cavity (fig. 1). *Staphylococcus* was again grown from the fluid. The wound was entirely open, exposing the anterior mediastinum. The pleural cavity was walled off and did not communicate with the wound. A roentgenogram showed bronchopneumonia of the base of the right lung in addition to the large bottle-shaped cardiac shadow and the radiopacity of the base of the left lung.

July 30: The cough increased and was aggravating. Only 50 cc. of fluid was obtained from the pericardial cavity; the fluid was lost, so culture was not obtained.

August 4: One hundred and fifty cubic centimeters of sterile fluid was aspirated from the pericardial cavity. The patient seemed stronger, but the temperature remained around 101 F.; the pulse rate was 140, and the respiration, 50.

thorax. The right side of the diaphragm was less active than the left. The heart was slightly globular (water bottle type), the enlargement being especially to the right. Fluid was not seen in the pericardium. The bullet was immediately to the left of the midline, moving with each heart beat and lying close to the anterior wall of the chest. Fluoroscopic examination two hours later did not show any change in the condition.

Operation was performed about three hours after admission by Dr. Victor Hill. A midline incision was made down to and through the sternum from the ensiform cartilage to the attachment of the fourth costal cartilage, where the incision was carried laterally through the left side of the sternum into the fourth interspace. When the left portion of the sternum was retracted, the pericardium was exposed. This was incised and retracted, and there was little fluid in the pericardial cavity. A darkened area could be seen on the anterior portion of the right ventricular wall where the bullet could be felt deep in the heart. A suture was placed in the apex of the heart for traction, according to the technic described by Beck.¹³ A suture was then placed in the heart muscle on either side of the bullet. The bullet was removed with a hemostat and a large stream of blood spurted from the wound. The two sutures that had been placed on either side of the wound were then pulled to the opposite side from which they were placed, which thoroughly controlled the bleeding. The wound was then closed with interrupted figure-of-eight silk sutures. (Six of these sutures were used.) The pericardium was closed with interrupted sutures of silk. The sternal reflection was put into place and sutured with kangaroo tendon.

The temperature rose to 103 F. the following day, the pulse steadily increased in rate and became weaker. There were moist râles in the right lung; the left lung seemed clear, but sounds were distant. The patient reacted poorly, and died forty-eight hours following operation.

Postmortem examination showed only a small amount of fluid in the pericardium. The sutures in the heart muscle were removed. The wound extended a distance of 15 mm. into the interventricular septum with a lateral perforation into the cavity of the right ventricle. The left lung was collapsed and airless. There was a slight diminution of crepitation in the right lung.

CASE 2.—H. M. A., a colored man, aged 26, was admitted to the Louisville City Hospital on July 16, 1927, with a stab wound 8 cm. in length and extending from the tip of the ensiform cartilage slightly upward and to the left. The patient presented the general picture of shock: The pulse was 160 and weak; the skin was cold and moist; every time he breathed a slushing sound was produced, and considerable blood was sprayed from the wound. He was under the influence of alcohol, which may have contributed toward his semiconscious condition.

An attempt was made to combat shock by subcutaneous infusion of saline and caffeine sodium benzoate, application of external heat and hot coffee by rectum.

After the patient was in the operating room, which was about two and a half hours following the accident, examination showed that the tip of the ensiform cartilage and the cartilages of the fifth, sixth and seventh ribs were cut. Although this opening, which was already made, gave a rather low exposure of the heart, it was fairly satisfactory. The skin and subcutaneous tissues surrounding the injured area were infiltrated with 1 per cent procaine hydrochloride, no other

13. Beck, Claude S.: Wounds of the Heart. *Arch. Surg.* 13:205 (Aug.) 1926.

digitalis, limitation of the fluid intake and methods favoring the excretion of fluids. Merbaphen was given repeatedly at from two to five day intervals; a large output of urine followed the use of this drug, and there was a noticeable reduction of edema.

Edema was not noticeable after October 7. The wound had healed. The fluid intake was gradually increased, and was well tolerated. Antisyphilitic treatment was started.

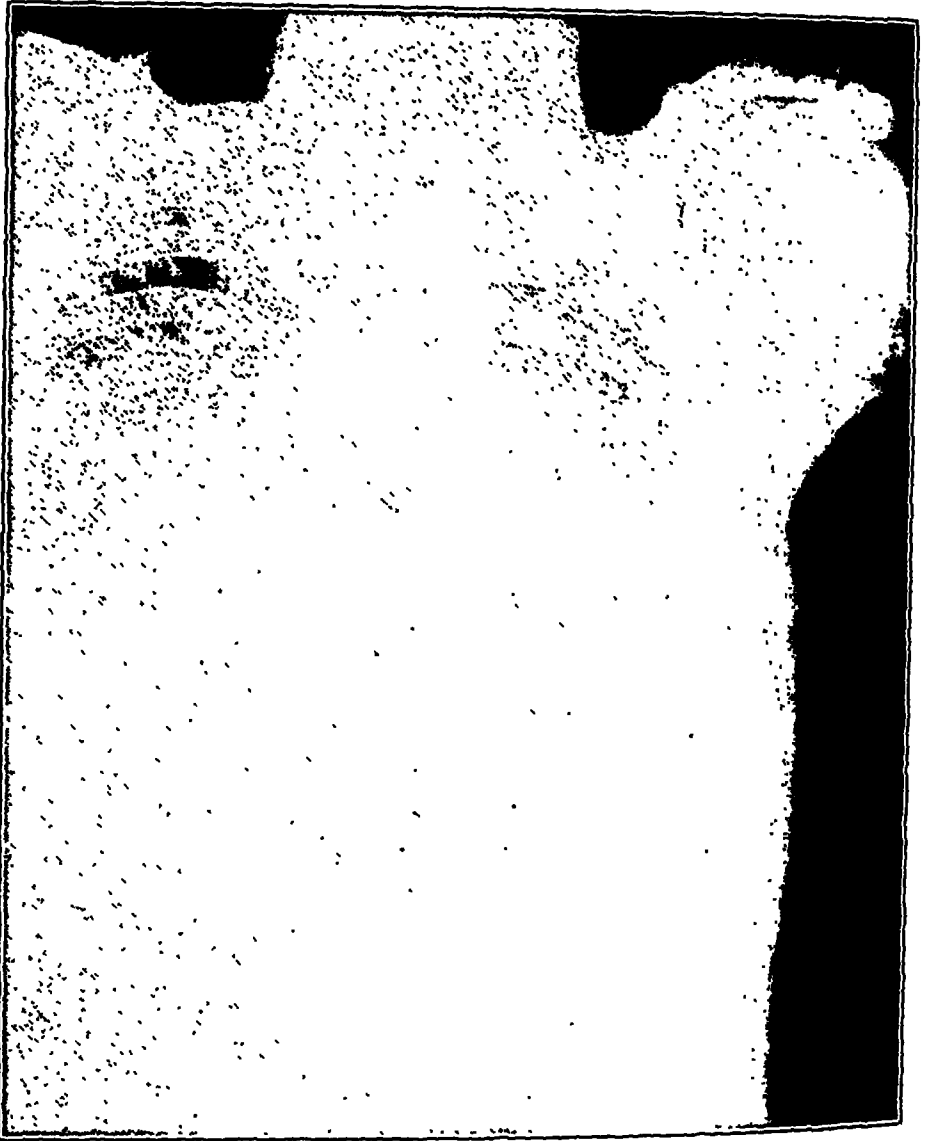


Fig. 2.—Roentgenogram taken Aug. 22, 1927, showing fluid in both pleural cavities.

October 20: The patient was allowed out of bed. He would not take exercise gradually, but walked about at will the second day he was up; he did not suffer any ill effects, and continued to go about as a normal person.

October 30: He was discharged from the hospital in apparently good physical condition; the fields of both lungs were clear, and his heart was 12 cm. in its greatest diameter (fig. 3).

November 9: He was seen for the last time, and seemed normal.

August 13: One hundred and fifty cubic centimeters of sterile fluid was aspirated from the pericardial cavity. The temperature was 100 F.; the pulse rate, 120, and respiration, 40. The patient's condition was much better, although he continued to have an irritating cough. The chest wound was clean and granulating.

August 20: The patient was so well that he was allowed to sit up for a short while. The temperature had been normal for six days previously.

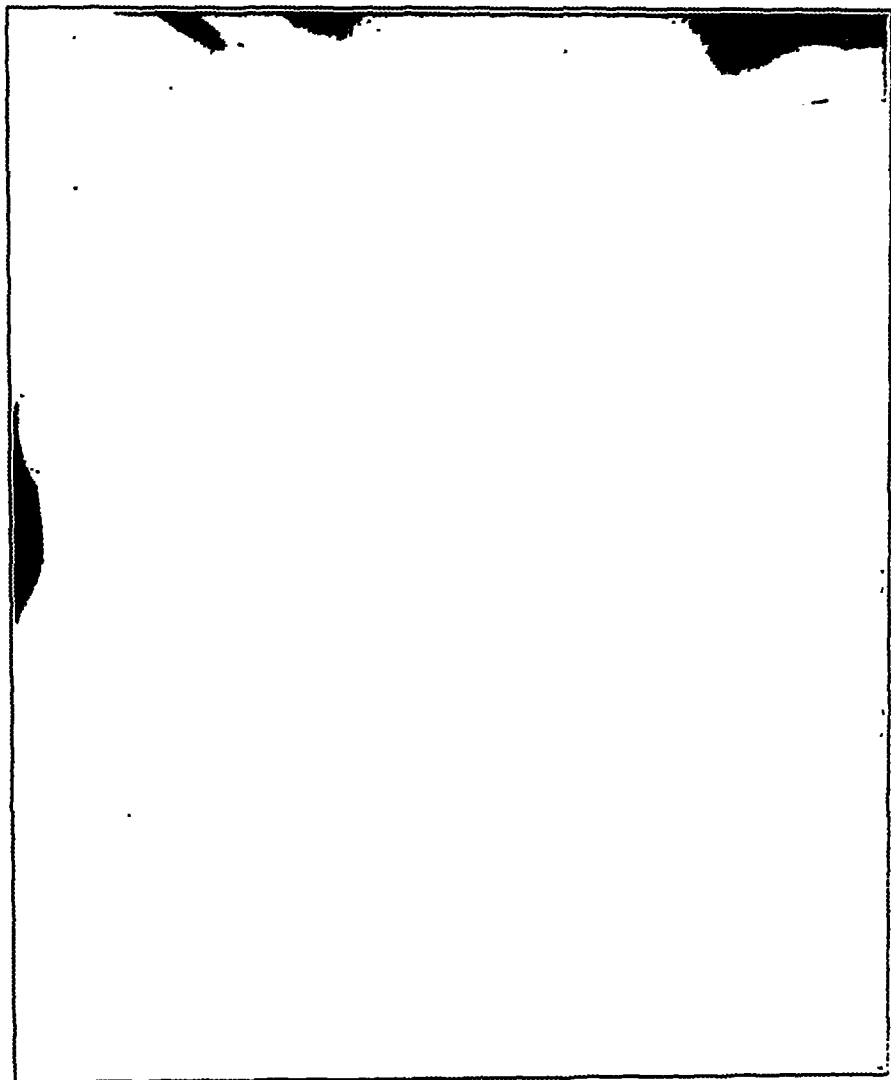


Fig. 1.—Roentgenogram taken July 26, 1927, showing enlargement of the cardiac shadow, bronchopneumonia at the base of the right lung and radiopacity of the base of the left lung.

August 22: Dyspnea and generalized anasarca was found on examination (fig. 2).

During the next six weeks, general treatment was given for cardiac decompensation, the etiology of which was considered to be myocardial injury, adhesive pericarditis or both. The treatment in general consisted of the administration of

irritant to the pericardium cause either pericardial effusion or adhesions or both. Small amounts of blood would be injected into the pericardial cavity, the blood would be absorbed, and effusion or adhesions did not develop. These experiments bring out forcibly that it is most important to produce as little trauma as possible. The sponging of the blood from the cavity with gauze produces trauma and suction should be substituted when possible.

The associated pneumothorax may be a factor in lowering the resistance of the patient. Therefore, when feasible, it would seem advantageous to close the thorax tight and remove the air from the pleural cavity.

Aspiration of the pericardial cavity is a procedure not entirely free from danger. A coronary artery may be punctured, the pericardial cavity becoming filled with blood, and fatal tamponade result. Owing to this possibility—such an accident has occurred—suppurative pericarditis should be treated by open incision when the condition of the patient warrants that procedure. Ordinarily, the best location for the insertion of the needle, when aspiration is to be performed, is just below to the left of the ensiform. This is the only location where the pericardial cavity may be entered without penetration of the pleural cavity. This location was not selected in my case, because the obviously infected wound was at that site.

NOTE.—The patient returned to the hospital on May 1, 1928, in perfect health. He said that he had not had any cardiac embarrassment since leaving the hospital.

COMMENT

The method of handling the heart by the traction suture in the apex enables the procedure to be carried out with much less trauma than by any other method now known. The placing of sutures alongside the wound to control hemorrhage prevents soiling of the operative field.

Many of the early operators left a drain in the pericardial cavity. Adhesive pericarditis almost invariably followed these cases. In most of

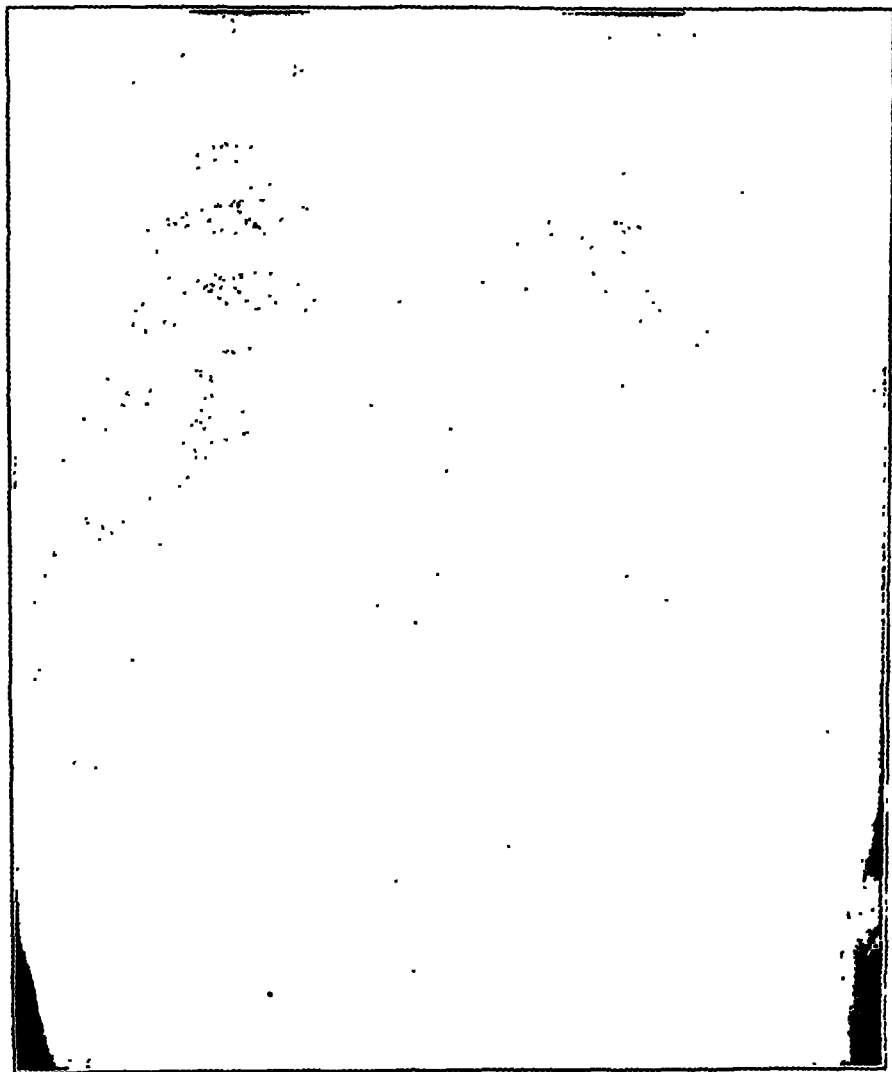


Fig. 3.—Roentgenogram of patient just before leaving hospital on Oct. 30, 1927, showing a return to almost normal.

those cases in which drainage was not used, pericardial effusion developed. These observations led to some experimental work by Beck and Moore,¹⁴ who found that mild trauma and the application of a chemical

14. Beck, C. S., and Moore, R. L.: The Significance of the Pericardium in Relation to Surgery of the Heart, *Arch. Surg.* 11:550 (Oct.) 1925.

that the tendon of the long head was not congenitally absent, but that it had secured a secondary attachment after division. Since neither my associates nor I have seen a single convincing case of congenital absence of the tendon of the long head in adults, in more than a thousand arms, it is clear that this condition is rare, although absence of the long head is common. Indeed, the high incidence of the latter itself compels another interpretation than that of developmental anomaly alone.

In previous publications,⁶ I have tried to convey the idea that partial or complete destruction of the articular portion of this tendon is relatively common and not unique, as King and Holmes⁷ seem to imply.



Fig. 1.—Left scapula, illustrating the apparently total fusion of the long head of the biceps with the dorsal portion of the ligamentous lip.

I have thirty-nine examples of dislocation and twenty of complete absence of the articular portion of this tendon in my possession at present. Although only six of the cases of dislocation are maximal, cases in which the tendon had passed completely over the lesser tuberosity,

6. Meyer, A. W.: Unrecognized Occupational Destruction of the Tendon of the Long Head of the Biceps Brachii, *Arch. Surg.* 2:130 (Jan.) 1921; Further Observations Upon Use-Destruction in Joints, *J. Bone & Joint Surg.* 4:491, 1922; Spontaneous Dislocation of the Tendon of the Long Head of the Biceps Brachii, *Arch. Surg.* 13:109 (July) 1926; footnote 1.

7. King, Jennings M., and Holmes, George W.: The Diagnosis and Treatment of Painful Shoulders, *J. A. M. A.* 89:1956 (Dec. 3) 1927.

SPONTANEOUS DISLOCATION AND DESTRUCTION OF TENDON OF LONG HEAD OF BICEPS BRACHII

FIFTY-NINE INSTANCES *

A. W. MEYER

PALO ALTO, CALIF.

In bringing these two conditions together in the title, I am not assuming that they necessarily are always associated and that every case of destruction of this tendon necessarily was first one of dislocation. In most cases, however, dislocation of the tendon probably leads to greater wear, but, as reported previously,¹ tendons still lying in a normal position and in otherwise normal shoulder joints may show considerable wear.

Since the biceps as well as other muscles may be congenitally absent, it follows that the tendon of either head may also be absent congenitally, but it is improbable that all the statements in the literature on this matter can be taken at their face value. I never have seen a clear case of congenital absence of the long head since I have understood the condition better, and few of those reported in the literature, including my own,² are absolutely convincing in view of the facts I have subsequently revealed. Such cases as those spoken of by Lauth³ and Lecco⁴ seem unequivocal, but what is needed is examination of the tendon in a large series of the new-born.

I do not believe that the prominence of the supraglenoid tubercle is a reliable criterion for deciding whether the tendon of the long head is congenitally absent; for, as shown in figure 1, the tendon of the long head frequently merges so completely with the ligamentous, glenoidal lip as to be indistinguishable and also inseparable from it. One could therefore expect great variations in the prominence of the tubercle for this reason alone. In such cases as that reported by Craig,⁵ the downward extension of the so-called transverse humeral ligament suggests

* From the Department of Anatomy, Stanford University.

* This does not include a number of instances in the twenty-five bodies under dissection this year.

1. Meyer, A. W.: Further Evidences of Attrition in the Human Body. *Am. J. Anat.* 34:241, 1924.

2. Meyer, A. W.: Absence of the Tendon of the Long Head of the Biceps. *J. Anat. and Phys.* 48:....., 1913-1914.

3. Lauth, Ernest Alexandre: *Nouveau manuel de l'anatomiste*, Paris, 1829.

4. Lecco, T. M.: Ein Fall von vollständigen Fehlen des langen Kopfes des M. biceps brachii und die damit in Zusammenhang stehenden Veränderungen an Knochen und Gelenktheilen, *Anat. Anz.* 1907, vol. 30.

5. Craig, Joseph D.: Anomaly of the Long Tendon of the Biceps Muscle of the Arm, *New York M. Record*, 1899, vol. 56.

published a photograph (fig. 7) of a relatively early case without interpreting it as such. The paired humeri represented in figure 2 illustrate a still earlier stage in a case of dislocation. The condition of the sulcus on the left humerus represents an earlier stage than that on the right, for in the latter the tendon had already left the proximal part of the sulcus and had come to play on its anterior wall and crest and on the lesser tuberosity. In all the cases of dislocation I have seen, the tendon still occupied the sulcus in the region distal to the tuberosities. As the sulcus is shallow here, it is difficult to see how it would be possible to determine the absence of the tendon by palpation, and those



Fig. 2.—Paired humeri, illustrating instances of beginning dislocation. The widening of the proximal portions of the sulci should be noted.

who have claimed that they have found the sulcus empty in the living, must of necessity have determined this by palpation through skin, subcutaneous tissues, fasciae and the thick layer of muscles (pectoralis major and deltoid) overlying the more proximal portion of the sulcus, which is the only region in which dislocation is known to occur spontaneously; that is, gradually from use.

Since the bodies used in the anatomic laboratory at Stanford University are not drawn from an unusual source but represent the classes and occupations usually represented in this material, I see no reason why the incidence of bicipital dislocation in this laboratory should be

most all of the rest are wholly unequivocal to any one familiar with the condition. In all the cases of absence of the articular portion, the tendon had obtained a secondary attachment to the floor or sides of the sulcus or to the humeral diaphysis directly distal to the lesser tuberosity, as represented in figures 4, 5 and 6.⁸

Although complete absence of the intra-articular portion (destruction) occurred more frequently on the right than on the left, the opposite is true of dislocation; however, since both series still are small, not much importance can be attached to conclusions drawn from them. Thirteen cases of complete destruction occurred on the right and seven on the left, and seventeen cases of dislocation occurred on the right and twenty-two on the left. Both sexes are represented, and in four cases the dislocation was bilateral. As I did not preserve all cases of destruction of the tendon because they are so common, and did not discover such a possibility as spontaneous dislocation until a few years ago, it is probable that I will be able to extend these observations considerably during the next few years. Many cases probably were overlooked.

I realize that the word spontaneous is out of place here as elsewhere, but I am using it to distinguish these cases of dislocation from those resulting from sudden trauma due to exertion or to external causes. Some trauma undoubtedly is associated with these cases of gradual occupational dislocation, but trauma, in the ordinary sense, is not a factor. Nor do I wish to rule out chronic arthritis. Evidences of its presence are unmistakable in some cases, but there is no reason to suppose that people afflicted with chronic arthritis thereby become immune to dislocation. They would, of course, be more likely to suffer it because of the changes in bone and capsule associated with this disease.

In some cases in which the divided tendon obtained a secondary attachment to the diaphysis distal to the lesser tuberosity, it may have been dislocated and have played on the tuberosity before it was divided; hence it is possible that most of these cases should really be included among cases of dislocation. It is not improbable that this also is true of the cases in which the tendon is attached to the floor of the sulcus in the region of the lesser tuberosity, for it is not necessary for the tendon to be exposed to considerable wear from contact with the relatively rough face of the lesser tuberosity, in order to be weakened by wear.

PARTIAL DISLOCATION

Since the observations published in 1926, I have found that partial dislocation of this tendon is a far commoner condition in bodies in our dissecting room than I had surmised. As stated at that time, I did not recognize the cases of beginning dislocation at first, and in 1924, I

8. Meyer (footnote 6, first reference).

The relation of the tendon to the head of the humerus, and to the floor of the intertubercular sulcus, necessarily changes as the position of the arm changes, for both shift beneath it. When the arm is in slight lateral rotation, the under surface of the tendon lies fully on the floor of the sulcus; but as lateral rotation is increased, its anterior margin is forced against the anterior wall of the sulcus, especially that portion formed by the lesser tuberosity and the capsular attachment proximal to it. In medial rotation, on the other hand, the anterior wall of the sulcus and the adjacent capsular attachment become the surfaces which the tendon uses as a trochlea, while its dorsal margin is forced against the dorsal wall of the sulcus.

It is evident that the tension exerted on the capsular attachment proximal and superior to the lesser tuberosity varies with the position of the arm and the disproportion in width between the tendon and the sulcus, as well as with the force exerted by the muscle on the tendon. It seems probable that the greatest tension is exerted on this portion of the capsule which is the first and chief obstacle to forward dislocation especially in the position of extreme lateral rotation during partial abduction. This is the position frequently reached in occupations that require shoveling. In extreme abduction the relations would be entirely different, and the tendency to dislocation would probably be slight because of the approximation of the lesser tuberosity to the supraglenoid tubercle.

The tendency to dislocation of this tendon, which exists in all normal shoulder joints, is opposed primarily by the attachment of the articular capsule in the region proximal to the lesser tuberosity. Contrary to the usual statement, I do not believe that the so-called transverse humeral ligament is an important factor for preventing dislocations, for I have seen cases in which the tendon was entirely normal in position, although this ligament was extremely weak or absent. Moreover, after observing the condition of the intertubercular portion of the capsule, I fully concur in the omission of a name for this so-called ligament from the Basle nomenclature. Transverse fibers bridging the sulcus, which could be designated properly as a ligament, seldom are present, and when this is the case, they usually are located farther distally than the intertubercular region, in which the transverse humeral ligament of Brodie is supposed to occur.

I have seen only one case of complete ossification of the intertubercular portion of the capsule and another in which ossification was partial. In the former, the tendon passed through a bony canal about 2 cc. long as in the mole, armadillo and musk ox, and in the latter case it was covered medially by an exostoses. It is such rare instances as these that may have phylogenetic significance and hence justify the term transverse humeral ligament, but careful developmental and statistical studies are necessary to establish this.

unusual. With a few exceptions, practically all the bodies are of persons who belonged to the working classes. The great majority were Caucasian, only a few having been negroes, Chinese, Mexican and Hindus.

The greater frequency of absence of the intra-articular portion of the tendon on the right side may be due to right-handedness, and the somewhat larger frequency of dislocation on the left may be due to the fact that greater tension is put on the tendon and the capsular attachment on this side, in occupations that require shoveling and pitching with a fork, for the left hand acts as fulcrum and the left humerus passes into marked lateral rotation and abduction in every such movement.

†

ANATOMIC FEATURES

In considering the anatomy of the humeroscapular articulation, one is impressed with the fact that the normal conditions promote dislocation of the tendon of the long head. Until the arm is abducted somewhat, the tendon curves forward, encircling the slippery and sloping, rounded surface of the upper, anterior portion of the head of the humerus. As tension on the tendon is increased, it tends to displace the latter backward and downward. This does not imply, however, that a gap, such as appears in roentgenograms of the shoulder with the arm at rest, exists between the head of the humerus and the acromion. Muscle tone alone always must keep these in contact. The large gap seen in roentgenograms of the shoulder is due, of course, to the presence of the articular cartilage and capsule and the tendon of the supraspinatus, and is magnified because the lower surface of the acromion and the cartilage on and the underlying compacta of the humeral head, are curved bodies. Since the humero-acromial interval is decreased decidedly in all cases of destruction of the upper portion of the capsule and the tendon of the supraspinatus and also by wear on the under surface of the acromion and on the articular cartilage of the humeral head, this decrease should be evident in roentgenograms.

Although the articular cartilage on the humerus is sometimes grooved slightly by the tendon in the region adjacent to the tuberosities, this sulcus is too shallow to have much, if any, influence in maintaining the normal position of the tendon, and only that portion which lies between the tuberosities in adduction, is properly accommodated by the normal sulcus. The tendon usually widens and flattens decidedly as the supraglenoid tubercle is approached, where it sometimes is three, or more, times as wide as in the intertuberosital portion, when the arm is at rest. Since anatomists now speak of the entire bicipital sulcus as intertubercular, I am using the word intertuberosital to designate the portion between the greater and lesser tuberosities.

present, (5) the capsular attachment may be weakened by intracapsular bursae and (6) the capsular attachment to the anatomic neck in the region proximal to the lesser tuberosity may be restricted.

INTRAMURAL BURSAE

So far as I know, the presence of bursae in the capsular attachment in this region has not heretofore been reported; yet, not infrequently, one or two small intracapsular suprapariosteal bursae are present. The presence of these bursae in this region of capsular attachment results in the weakening of it. I am not certain as to the genesis of these bursae, but I do not believe that they are congenital, but rather that they result from the play of the tendon of the long head against and on this portion of the capsular attachment, especially during marked lateral rotation. Not infrequently the bursa of the subscapularis also extends far up under the tendon of this muscle, and it may even communicate with the sheath of the long head in the intertubercular sulcus. This may also be the case with the intracapsular bursa or bursae which form a gap bridged by the capsule or the tendon of the subscapularis, as the case may be. Such defects in the capsular attachment must greatly facilitate dislocation of the tendon, for they weaken the primary obstacle against its inception. Although the articular capsule and the tendon of the subscapularis always fuse intimately, it is only the capsular attachment which is an obstacle to dislocation, for the dislocated tendon of the long head does not detach the tendon of the subscapularis but comes to lie on it in far advanced cases, as illustrated in the figures referred to. If the capsular attachment to the bone in this region is maintained and stretches, the tendon of the long head comes to lie in a capsular sling, as shown in figure 4. This necessarily protects it against attrition on the face of the lesser tuberosity. Under these circumstances, it may become dislocated without showing much or even any wear from contact with the lesser tuberosity, and such cases are not rare.

Since in all the cases of detachment of the tendon of the subscapularis over practically the entire lesser tuberosity some arthritic reactions are shown, it seems to me that the gradual dislocation of this tendon probably results from disease, although mechanical factors are involved. In some cases the tendon of the subscapularis retains an attachment anterior and distal (below) to the lesser tuberosity only, and looks as though it had undergone a slow migration from the region of its wide normal attachment. It must not be overlooked, however, that abnormalities in the attachment of this tendon may also be concerned in this matter.

Spontaneous dislocation of the tendon of the long head of the biceps may occur without the presence of arthritis, a supratubercular

The nature of the anterior wall of the sulcus necessarily is an important factor in dislocation. This applies especially to the presence or absence of the bony ridge shown in figure 3, which I have called the supratubercular ridge. Although this name might imply that it is related to either tuberosity, I have never seen it related to the greater. It extends obliquely forward and downward from the region of the articular cartilage to the upper and dorsal portion of the lesser tuberosity. As the surface of the distal extremity of this ridge is on a level with the surface of the latter, and since the tendon plays on it



Fig. 3.—Portion of a right humerus with a supratubercular ridge marked X.

much as the tendon of the peroneus longus plays on the trochlea of the cuboid, its rôle in dislocation is plainly evident. In a study made by Cilley (unpublished) it was present in 17.5 per cent of 200 humeri.

In all normal joints there are three, and there may be six, factors which favor dislocation of this tendon: (1) the normal course of the intracapsular portion of the tendon and its relation to the humeral head, (2) the much greater width of the proximal portion of the tendon, (3) the fact that the anterior wall of the sulcus which is formed by the lesser tuberosity normally acts as a trochlea for the tendon in the usual position of medial rotation, (4) a supratubercular ridge may be

Not infrequently the floor of the intertubercular sulcus slopes decidedly toward the greater tuberosity in its upper extent, thus tending to throw the tendon against the dorsal wall of the sulcus and facilitating wear on this margin, as shown in figure 5. The first instances of this kind which I saw led me to think that the wear of the tendon here must have resulted mainly from its being caught between the greater tuberosity and the acromion, after a defect had been formed in the articular capsule; but the subsequent finding of worn tendons in joints with intact, normal capsules made this interpretation untenable. I have also found that the tendon can be dislocated without previous detachment of the articular capsule, for the latter may merely stretch in the region of the lesser tuberosity instead of becoming detached.

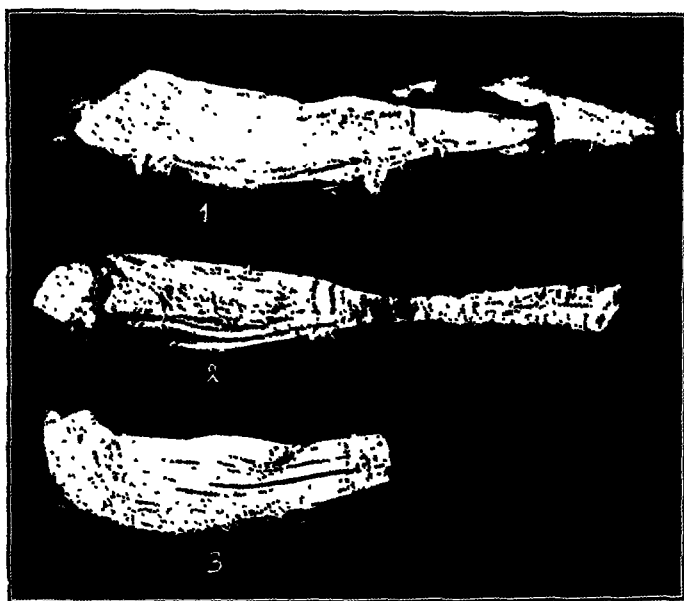


Fig. 5.—Three left bicipital tendons from otherwise wholly normal joints, showing wear along the dorsal margins. The reflection of the tendon sheath is clearly shown in number 1. All the tendons were cut close to their origin.

The fraying of its dorsal margin manifestly is produced by contact with the dorsal wall of the sulcus and is especially marked in tendons which are much wider in their proximal portions. Fraying of this edge may extend to within 0.5 cc. of the supraglenoidal attachment. I do not know whether or not wear on this margin, under otherwise normal conditions, would ever be sufficient to divide the tendon, but I am inclined to doubt it. It could, however, not fail to weaken it and thus facilitate its rupture.

In some cases in which the tendon had ruptured some distance from its place of origin, the proximal fragment could be recognized, although it had become adherent to the inner surface of the capsule. Often it

ridge or bursae in the region of the capsular attachment, and also without the restriction of this attachment to the upper margin of the lesser tuberosity. Although it must remain a matter of opinion as to just what constitutes beginning dislocation, I think it conservative to say that approximately 4 per cent of the bodies and 8 per cent of the



Fig. 4.—A right humeroscapular articulation with the tendon reflected anteriorly to reveal its bed. The proximal portion of the intertubercular sulcus is seen to the left of the new bed of the tendon. This tendon, which lies in a capsular sling, had passed practically over the lesser tuberosity but still occupied the sulcus distal to the intertuberosital region.

tendons illustrate some stage of this process. A sufficient number of these cases present no evidences of pathologic conditions to reflect arthritis as a primary or sole cause.

In view of the undoubted commonness of destruction and dislocation of the tendon of the long head of the biceps, it is especially regrettable that clinical histories are not available. This is no one's fault, of course, for it is unlikely that any of the persons so affected sought relief from conditions of long standing by seeking medical care during later years. Moreover, the medical staffs of relief homes, almshouses and insane asylums are too small to permit much attention being given to slight disabilities or aches felt by the aged. However, although they remained unknown until recently, the conditions nevertheless are of peculiar scientific interest and also of great practical importance, for they undoubtedly were sustained during the most active years of the person's life.

SUPERNUMERARY CAPSULAR HEADS OF THE BICEPS

While studying the humeroscapular articulation in specimens at hand, I found three cases in which the biceps had a third tendinous or capsular head. In two specimens with unruptured tendons, these tendinous cords arose from the tendon of the long head in the region of the lesser tuberosity and extended to the upper anterior and inner surface of the articular capsule. These cords fused completely with the inner surface of the capsule and gradually thinned out as they continued toward the region of the supraglenoid tubercle. They are, however, entirely distinct from the long head and have exactly the same structure, although the largest is only half as thick as the entire tendon. The presence of such a capsular head would tend to prevent too great a retraction of the long head when the latter is divided, and thus would facilitate its secondary attachment in the region of the lesser tuberosity. It also seems that the traction exerted on the capsule by it might cause discomfort if not pain, especially in cases in which the tendon of the long head had stretched because of weakening from attrition.

These capsular heads of the biceps mentioned by Moser, Henle and Welcker, left the posterior and upper surface of the main tendon in the region of reflection of the synovial sheath. The largest lay adjacent to the main tendon, but one of the smaller occupied a separate, superimposed compartment. The former could be traced along the under surface of the capsule as far as the ligamentous lip of the glenoid cavity, in the region of the supraglenoid tubercle, but they were an unmistakable portion of the tendon of the long head. In the third case the supernumerary tendon lay outside of the synovial sheath of the tendon of the long head, but joined the capsule in the same region as the others. It widened out considerably distally and apparently joined the tendon of the pectoralis major. Too much had been removed in dissection to enable me to follow it further distally, but since it was attached throughout its extent along

could not be traced without difficulty, and in some cases not at all. Its fusion with the capsule may be due to traumatism, and its atrophy to disuse.

Although the incidence of spontaneous dislocation—and destruction—in the general population undoubtedly is far less than in the material in the dissecting room, it must be exceedingly common in persons who work in lumber and construction camps and in mines. Although the condition here described is undoubtedly chronic, it must be more or less distressing, even if not disabling, until maximal conditions are reached. In cases in which the intertubercular sulcus has not undergone secondary changes which have resulted in narrowing or roughening of it, relocation of the tendon, if not too badly worn, would seem justifiable if the tendon can be secured against recurring dislocation. Little could



Fig. 6.—Right tendon of the long head photographed from beneath, showing maximal wear. This tendon was attached only by a fine strand marked x, in the normal region and shows wear all the way down to the region of the reflection of its synovial sheath.

be accomplished, however, by relocating such a tendon as shown in figure 6, though it could be fastened securely to the diaphysis so as to restore normal tension on it and thus prevent a certain amount of atrophy of the lateral portion of the muscular belly of the biceps.

Except in early stages, I doubt, however, whether much can be gained in muscular power by reattachment of the tendon of the supraspinatus, so commonly divided by attrition, or displaced dorsally in cases of attrition. To reintroduce what remains between the bony surfaces involved might merely reestablish former disabilities, for the shortened tendon and muscle would have to be stretched considerably and would again be subjected to disastrous wear unless the patient changed his occupation.

tuberosity, or to the floor of the sulcus in this region, or still more infrequently to both walls of the sulcus, a portion of the frayed tendon being drawn to each side by the tendon sheath in the region of reflection of the latter.

5. In some cases in which the tendon is divided near the supraglenoid attachment, it retracts completely before it obtains a secondary attachment, with great lengthening of the extracapsular portion—even up to 100 per cent—and marked atrophy of the lateral belly of the muscle and resultant asymmetry.

its dorsal border in the region of the intertubercular sulcus and was fused so completely with the fascia proximal to the tendon of the pectoralis major, it is unlikely that it had a muscular component distinct from the biceps, and even if it did these supernumerary tendinous heads are totally different than the well known third muscular head of the biceps so commonly present.

None of these capsular heads could have developed from a portion of the synovial sheath which became strengthened through tension made on it, and since the tendon of the long head develops wholly outside of the articular capsule, and completes its migration inward as late as the third month of prenatal life, it need not surprise one that a portion of it may become stranded and fuse with the articular capsule through which it must pass. Indeed, it seems as though the entire tendon should some time be found in an extracapsular position. As far as I know this has not been observed. The tendinous component which arose from the articular capsule and ended near the tendon of the pectoralis major, if not in it, seems comparable to the glenobrachial muscle of Gruber; but since the other capsular heads here reported are supernumerary, they differ from cases in which all of the tendon of the long head arises from the joint capsule. It seems probable to me that anomalies such as these well may give rise to symptoms and thus make diagnosis of obscure conditions of the shoulder still more difficult. Any one especially interested in these heads will find them considered by Welcker.⁹

CONCLUSIONS

1. Uncomplicated, partial or complete, spontaneous forward dislocation of the supratuberosital and intertuberosital portions of the tendon of the long head of the biceps, on to or over the lesser tuberosity as far as the tendon of the subscapularis, is common in laborers past middle life.

2. This dislocation may be due to gradual stretching, detachment or destruction of the capsule proximal to and in the region of the lesser tuberosity.

3. Wear of the tendon along its dorsal margin may occur in otherwise normal joints, but wear throughout its width probably is frequently due to contact with the lesser tuberosity in cases of dislocation, or with the greater tuberosity and acromion in the course of destruction of the dorsal portion of the articular capsule, unaccompanied by dislocation.

4. After division by attrition, the tendon usually obtains a secondary attachment to the humeral diaphysis immediately distal to the lesser

9. Welcker, Hermann: II. Ueber Muskelvarietäten, *Ztschr. f. Anat. u. Entwgsch.*, 1876, vol. 1.

Sherrington found that in the jejunum 40 cm. below the pylorus, the intrajejunal pressure varied between 2 and 4 cm. of water.

By a slightly different procedure, we have confirmed these observations of the normal intra-intestinal pressure in dogs, and at the same time we have noted something of the relationship of the intra-abdominal pressure to that within the intestine in which obstruction has been produced. We share the view of Emerson³ that a slight positive pressure normally exists within the abdomen, that it is dependent for the most part on the tonus of the abdominal musculature and that normal alterations are due chiefly to the contractions of the diaphragm, change in tonus of the abdominal wall and variations in the bulk of the abdominal viscera.

During the course of this study, we have made observations on the intra-intestinal pressure in some eighteen small dogs (from 8 to 12 pounds [3.6 to 5.4 Kg.]) in each of which simple intestinal obstruction had been artificially produced. The obstructions were made for the most part at two levels, one from about 4 to 6 inches (10.1-15.2 cm.) below the duodenojejunal junction, the other an equal distance above the ileocecal valve. In four animals, the obstruction was made in about the middle of the small intestine. Isolated intestinal loops were made in four other animals, and the pressure recorded within the loop.

TECHNIC

Except when otherwise stated, all animals were given $\frac{1}{4}$ grain (0.016 Gm.) of morphine and ether anesthesia before operation. As strict aseptic precautions were taken as possible. In each case the bowel was doubly clamped and cut across. The lower end was turned in by the Parker-Kerr method and reinforced by a double row of mattress sutures. The clamp was removed from the proximal portion of the bowel and its lumen opened into which the apparatus used was then placed. It consisted of a brass tube about 2 inches (5.08 cm.) in length, with an internal diameter of 3 mm. and a threaded external surface. A concave metal disk about 1.5 cm. in diameter was fixed at one end, and a rubber washer was placed over the disk. A small incision was made in the wall of the bowel about 2 inches proximal to the site of section. The free end of the tube was placed within the lumen of the intestine and brought out through the small incision. The disk fixed one end of the tube within the intestine. The end of the bowel was closed in the same manner as the distal portion. A piece of omentum was then placed over the tube, another rubber washer applied and a second concave metal disk screwed down over the whole, fixing the omentum and the wall of the bowel, not too tightly, between the two rubber washers. A short rubber tube was then attached to the end of the metal tube and brought out through the abdominal wall by a separate stab incision. A small metal clamp closed the rubber tube.

At varying intervals after the operation until the death of the animal, readings were made of the degree of intra-intestinal pressure, and graphic records of the

3. Emerson, Haven: Intra-Abdominal Pressures. *Arch. Int. Med.* 7:754 (June 15) 1911.

INTRA-INTESTINAL PRESSURE IN OBSTRUCTION*

J. C. OWINGS, M.D.

C. A. MINTOSH, M.D.

H. B. STONE, M.D.

AND

J. A. WEINBERG, M.D.

BALTIMORE.

The presence of a toxic substance within the lumen of the bowel in cases of intestinal obstruction has long been recognized, but the process by which it enters the system, if indeed it is absorbed, is a problem that is as yet unsolved. The observations of Stone and Firor,¹ in 1924, suggested the possibility that the changed intra-intestinal pressure might alter the intestinal permeability. Without attempting to investigate the latter problem, it appeared that a study of the degree of pressure within the lumen of the bowel during obstruction might be undertaken with profit.

Before attempting to determine the abnormal conditions, it was necessary to find out the normal intra-intestinal pressure and the relationship of the intra-abdominal pressure to that within the intestine. The physiology of the gastro-intestinal tract from a mechanical point of view reveals an extremely complicated conducting system. The stomach, serving as a reservoir, must receive and readily accommodate the food that arrives often in large volume. Function requires that this mass be stored with little change in the intragastric tension, or else we should experience constant dysphagia, lack of appetite, gastric uneasiness and pain. Sherrington² confirmed this and found that the intragastric pressure in an etherized dog over a period of twenty minutes was from $\frac{1}{2}$ to $\frac{2}{3}$ cm. of water. The stomach at this time contained portions of a previous meal, but after 450 cc. of water was put into the stomach through a cannula, the pressure rose only to 6 cm. of water and twenty minutes later had fallen to 4 cm. On the other hand, the small intestine has not such great volumes to handle, but receives the products of the antrum pylori in smaller amounts and over a longer period of time. Such being the case, we would expect an intra-intestinal pressure less than that within the stomach. In the experiment already mentioned,

* From the Department of Surgery, Hunterian Laboratory, The Johns Hopkins University.

* Aided by the Hartley Fund.

1. Stone, H. B., and Firor, W. M.: *Tr. South. Surg. & Gynec. Ass.* 87:172, 1924.

2. Sherrington, C. E.: *Brain* 38:151, 1915.

any great difference from those operated on under ether and, indeed, in the instance already mentioned in which the intra-intestinal pressure was higher than usual during the first twenty-four hours and reached 36 cm. of water in six hours, ether had been used. Over this early period, there was no regularity of peristaltic action, as was found subsequently.

During the second twenty-four hours of obstruction, the sustained pressure remained between 6 and 8 cm. of water, while the degree of

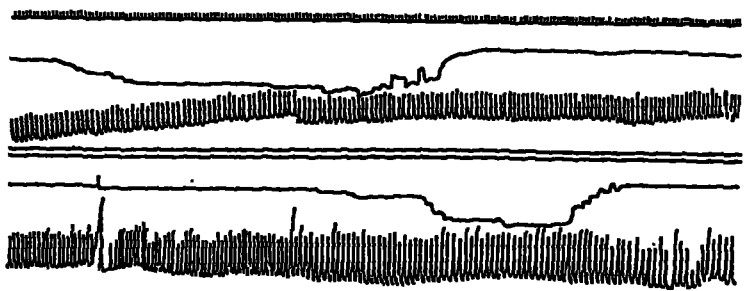


Fig. 2.—Tracing to illustrate the independence of the intra-intestinal pressure as compared with the respirations. Record of animal O. P. 15, in which obstruction had been produced in the lower part of the ileum for ninety-six hours; timer 3 seconds. A rise in the intra-intestinal pressure is represented on all the tracings by descent of the graph toward the bottom of the record.

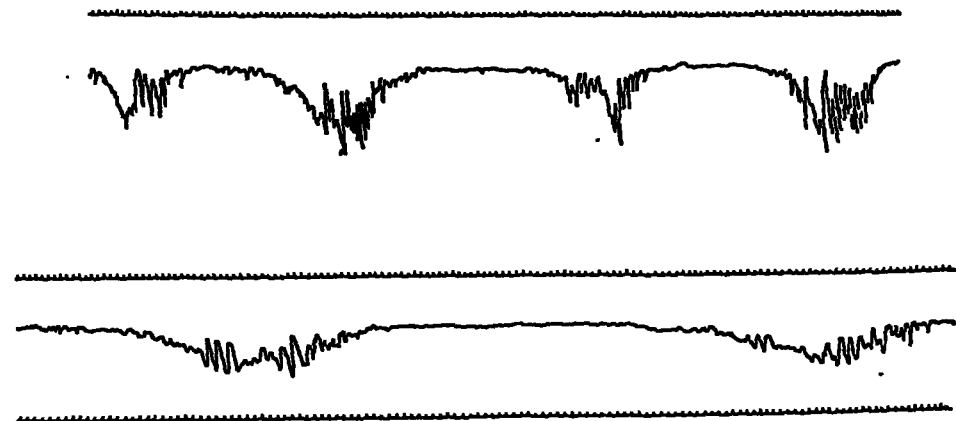


Fig. 3.—Graphic record obtained from one animal with a high intestinal obstruction and one with a low obstruction. The upper tracing is from animal O. P. 26, in which obstruction had been produced in the upper part of the jejunum for fifty-seven hours; the lower tracing is from animal O. P. 30, in which obstruction had been produced in the lower part of the ileum for fifty-two hours; timer 6 seconds.

pressure reached at the maximum of peristalsis rose considerably. In the dogs in which the high obstructions were produced, this pressure varied from 30 to 45 cm., while it generally took until the third day for the pressure in the dogs with low obstruction to reach the same-

motility of the bowel were obtained by a recording mercury manometer. Through a T-tube, a water manometer, 3 mm. in diameter, was attached in order to measure the lesser changes in pressure.

RESULTS

For the first twenty-four hours following operation, there was only a slight rise in the intra-intestinal pressure as a general rule, though in one case a considerable rise occurred within six hours. Usually

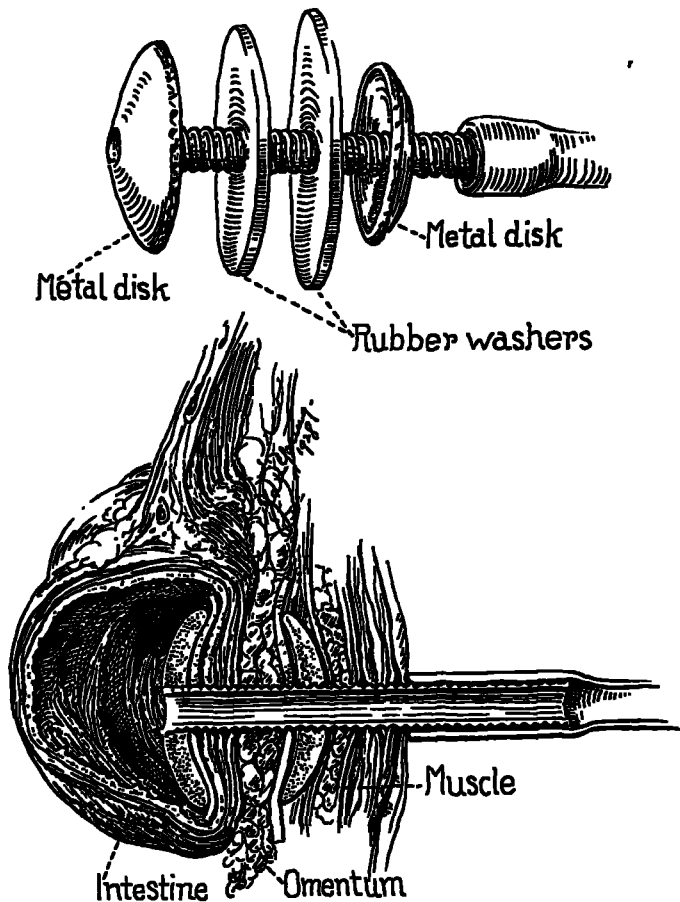


Fig. 1.—Drawing of apparatus described in technic is shown above; that of a cross-section of the apparatus in situ is shown below.

within twenty-four hours irregular peristaltic waves that reached a maximum of from 12 to 16 cm. of water were recorded. Between these there were inactive intervals during which the sustained pressure showed a gradual rise to 6 or 8 cm. As compared with the later observations, the bowel showed less activity during this early period probably owing, in the most part, to the operative trauma, the anesthesia and other factors. So far as the anesthesia was concerned, however, dogs in which obstruction was produced under procaine did not show

On the fourth day, the periods of increased pressure in the animals with high obstruction became less and less numerous, though the maximum level reached from 45 to 50 cm. of water. The sustained pressure began to decline, the toxicity of the animal increased quickly and death usually ensued about ninety-six hours after the obstruction. The dogs with low obstruction lived until the sixth or seventh day. The bowel showed good tone and considerable activity during the fourth and fifth days, after which fewer periods of increased pressure were noted and

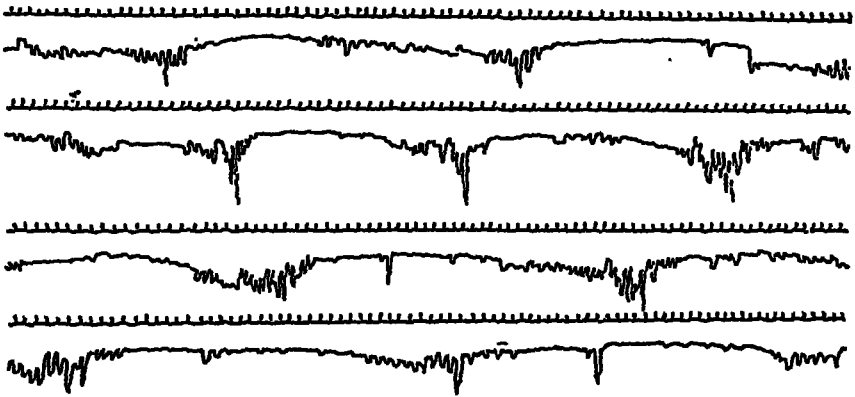


Fig. 6.—Record of animal O. P. 26 after obstruction had been produced for twenty-four hours; timer 6 seconds.

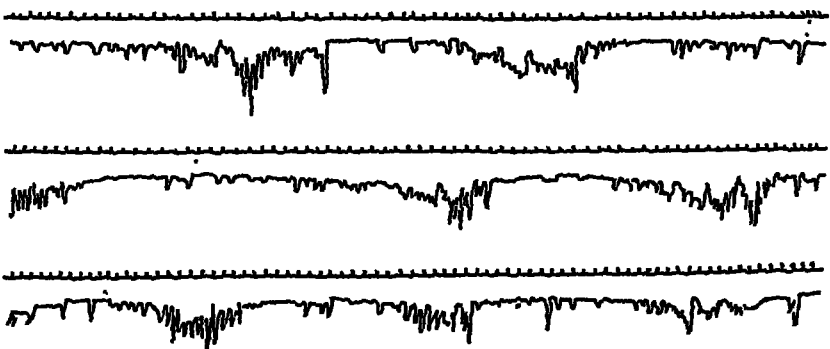


Fig. 7.—Record of animal O. P. 26 after obstruction had been produced for twenty-eight hours; timer 6 seconds.

the maximum level became less. The sustained pressure between these periods also diminished as the toxicity increased. During the twenty-four hours preceding death, the graphs showed slight undulations as the only evidence of intestinal motility.

The degree of pressure, then, within the lumen of the bowel in obstruction is greatly increased over the normal. The maximum levels in animals with high and low obstruction do not show great differences. The pressure rarely rises above 50 cm. of water, though in one isolated

level. The regularity of the peristaltic action became striking during this same interval. The periods of increased pressure in animals with high obstruction occurred about every third minute and lasted for about two minutes. In the animals with low obstruction, the regularity of action came on from forty-eight to seventy-two hours after the operation and the periods of increased pressure occurred every five to six minutes and lasted about three minutes. In other words, the periods of peristaltic action are more frequent in animals with high obstruction, and the graphic record obtained differed from that made in animals with

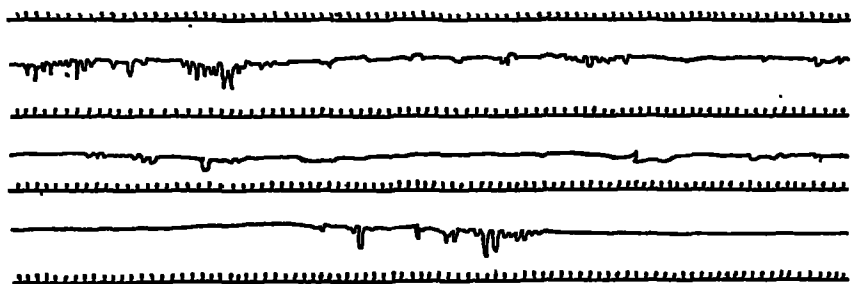


Fig. 4.—Graphic record from animal O. P. 26, after obstruction had been produced in the upper part of jejunum for four hours; timer 6 seconds.

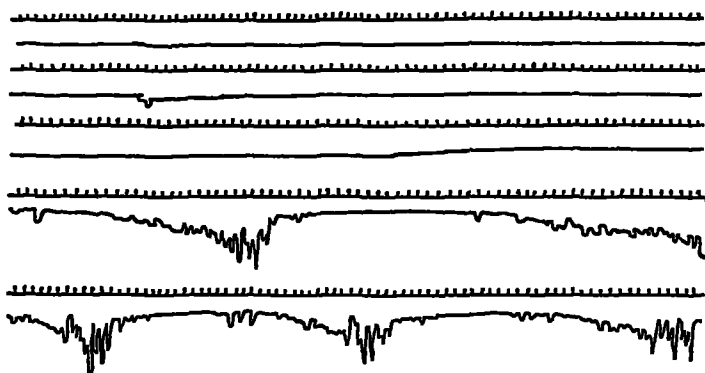


Fig. 5.—The upper three tracings show results in animal O. P. 26, after obstruction had been produced for ten hours; the lower two tracings, after twenty-two hours of obstruction; timer 6 seconds.

low obstruction in that a shorter time was taken for the pressure to reach its maximum. This is best shown in the kymographic records (fig. 3). The lower tracing, from an animal with low obstruction, shows a gradual increase in pressure with little irregularity until after the maximum is reached. The upper record, on the other hand, shows an abrupt or moderately abrupt rise in pressure with considerable irregularity. The fall in pressure in each case is much the same, showing marked evidence of peristaltic action, though somewhat more prolonged in the record made on animals with low obstruction.

instance a pressure of 58 cm. was reached. When accompanied by retching, vomiting or straining, the pressure is greatly increased and will reach above 100 cm.

In two instances, the intra-abdominal pressure was determined along with the intra-intestinal pressure. This was done by means of small soft rubber bags that were filled with water and placed within the abdomen; a connection was then made to a water manometer. A slight positive pressure was present when the animal was lying down; it measured from 1 to 4 cm. On deep inspiration, this level reached 8 cm. These variations were independent of the intra-intestinal pressure.

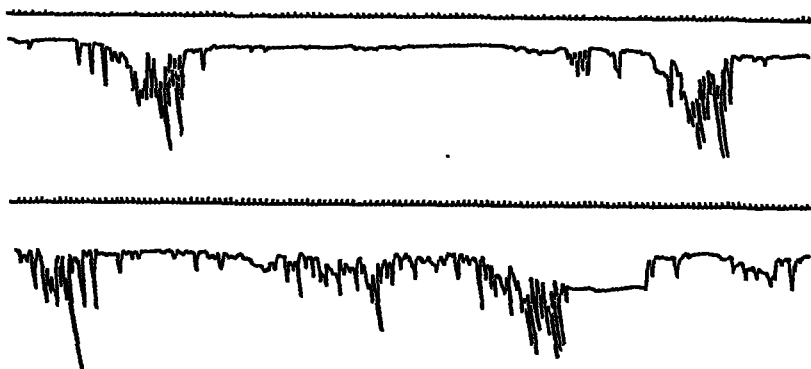


Fig. 11.—Record of animal O. P. 26 after obstruction had been produced for seventy-five hours; timer 6 seconds.

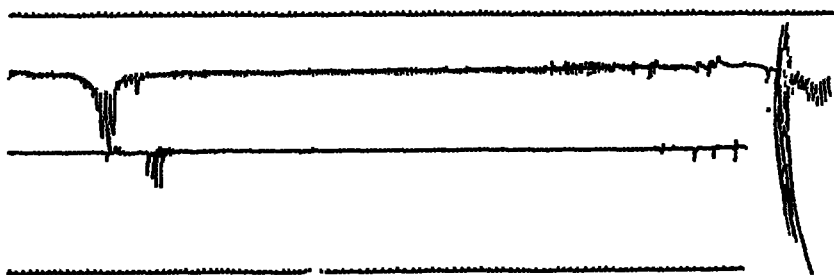


Fig. 12.—Record of animal O. P. 19 in which obstruction had been produced in the upper part of the jejunum for one hundred and thirty hours. Animal was moribund. Results show effect of respirations and vomiting; timer 6 seconds.

That the changes in the latter pressure are independent of the respirations is shown in figure 2. Extreme changes in intra-abdominal pressure, resulting from retching, vomiting and other conditions, however, are readily transmitted to within the lumen of the bowel (fig. 12).

In four instances, the pressure was measured within the lumen of isolated portions of the intestine. In three cases, these loops were made up of portions of duodenum and jejunum and in one instance of jejunum alone. Within the first twelve hours in all cases, the pressure

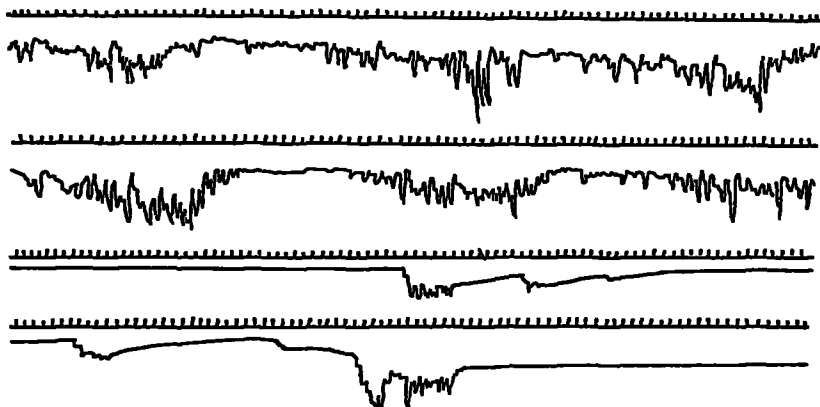


Fig. 8.—The upper two tracings show record of animal O. P. 26 after obstruction had been produced for thirty-three hours; the lower two tracings, after forty-eight hours; timer 6 seconds.

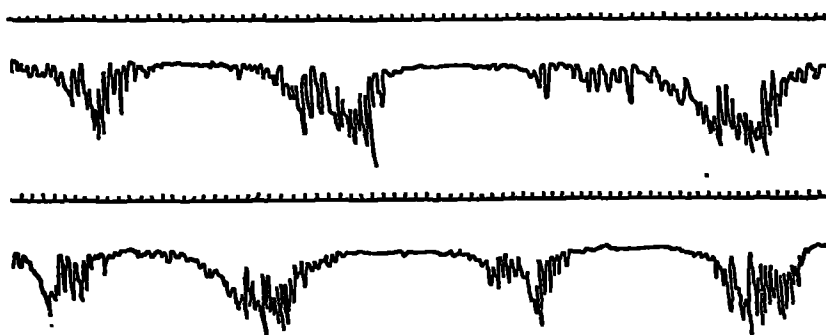


Fig. 9.—Record of animal O. P. 26 after obstruction had been produced for fifty-seven hours; timer 6 seconds.

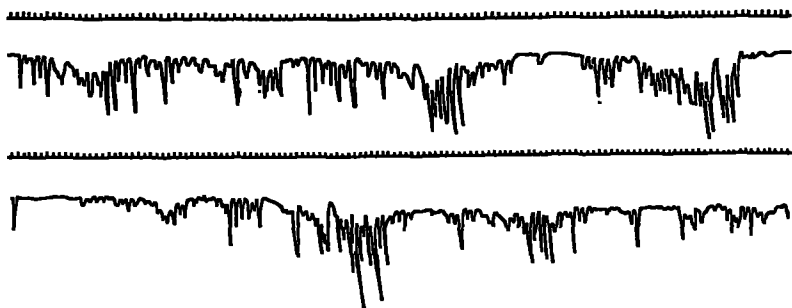


Fig. 10.—Record of animal O. P. 26 after obstruction had been produced for seventy-one hours; timer 6 seconds.



Fig. 16.—The upper tracing shows record from animal O. P. 17 after obstruction had been produced for ninety-six hours; the lower tracing, after one hundred hours; timer 3 seconds.



Fig. 17.—Record from animal O. P. 17 after obstruction had been produced for one hundred and twenty-four hours; timer 3 seconds.

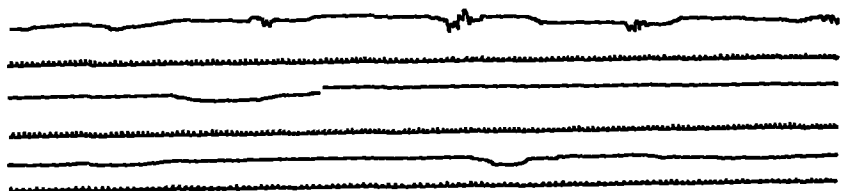


Fig. 18.—Record from animal O. P. 17 after obstruction had been produced for one hundred and fifty hours; timer 6 seconds.

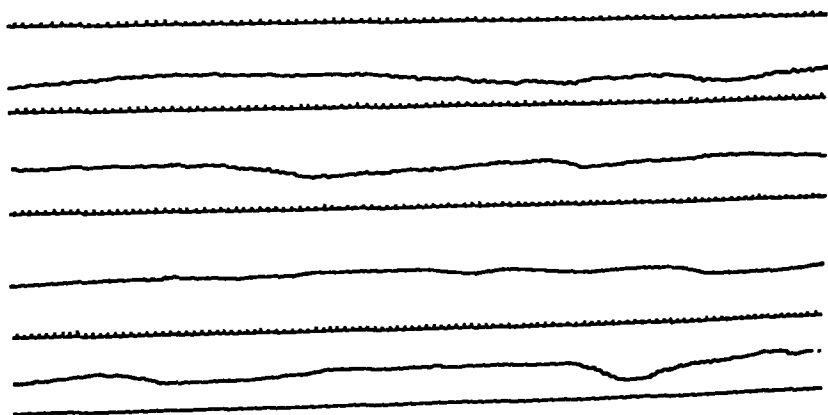


Fig. 19.—The upper two tracings show record from animal O. P. 17 after obstruction had been produced for two hundred and sixteen hours; the lower two tracings, after two hundred and twenty-one hours. The results show effect of fecal fistula; timer 6 seconds.

had risen to at least 30 cm. of water, and by twenty-four hours it had reached about 50 cm. The rhythmic periods of increased pressure were likewise present, and the sustained pressure between them showed a high tension, measuring from 16 to 18 cm. The sustained pressure

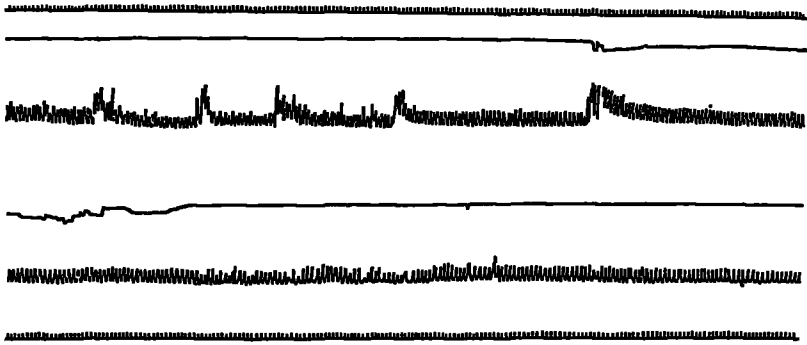


Fig. 13.—Graphic record from animal O. P. 17 in which obstruction had been produced in the lower part of the ileum for twenty-four hours. Respirations were recorded; timer 3 seconds.

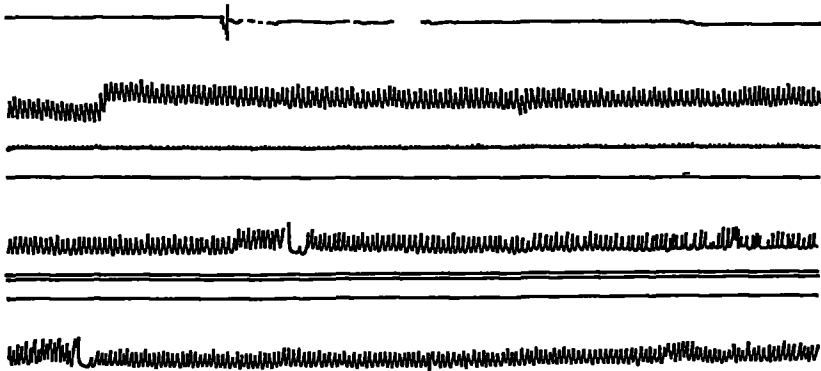


Fig. 14.—Record from animal O. P. 17 after obstruction had been produced for forty-eight hours. Respirations were recorded; timer 3 seconds.



Fig. 15.—Record from animal O. P. 17 after obstruction had been produced for seventy-six hours. Respirations were recorded; timer 3 seconds.

was maintained at a higher level than in the animal with simple obstructions and did not fall off until perforation occurred. The maximum pressure observed was 70 cm. of water. The length of life in these animals was from twenty-nine to forty-eight hours. Three died from general peritonitis resulting from a perforation of the loop at the

TABLE 2.—*Protocol of Dog O. P. 17*

| Period of Observation | Hours Obstructed | Maximum-Minimum Pressure, Cm. Water | | Notes |
|------------------------------|---------------------|--|---------|---|
| | | Maximum | Minimum | |
| Feb. 10—11:00-12:00 a. m. | ... | .. | .. | Operation; $\frac{1}{4}$ grain morphine; ether; obstruction lower part of ileum |
| 4:00- 4:15 p. m. | 4 | 14 | 10 | |
| Feb. 11—11:00-12:00 a. m. | 24 | 18 | 7 | Fig. 13 |
| 10:00-11:00 p. m. | 35 | 18 | 7 | |
| Feb. 12—12:00- 1:00 p. m. | 49 | 9 | 5 | Fig. 14 |
| 4:00- 5:00 p. m. | 52 | 12 | 8 | |
| Feb. 13—11 a. m.-12:30 p. m. | 72 | 36+ | 7 | |
| 3:00- 4:00 p. m. | 76 | 44 | 5 | Fig. 15 |
| Feb. 14—10:30-11:15 a. m. | 96 | 40 | 8 | Fig. 16 |
| 3:00- 4:00 p. m. | 100 | 28 | 8 | Fig. 16 |
| Feb. 15—12:00- 1:00 p. m. | 121 | 20 | 6 | |
| 2:30- 4:00 p. m. | 124 | 30 | 6 | Fig. 17 |
| 8:30- 9:30 p. m. | 130 | 24 | 8 | |
| Feb. 16—10:00-11:30 a. m. | 144 | 16 | 6 | |
| 3:45- 5:15 p. m. | 150 | 24 | 10 | Fig. 18 |
| 8:30- 9:30 p. m. | 154 | 18 | 10 | |
| Feb. 17—11:00-12:00 a. m. | 168 | 18 | 8 | Fecal fistula |
| 4:30- 6:00 p. m. | 174 | 30 | 2 | |
| 8:45-10:00 p. m. | 177 | 16 | 8 | |
| Feb. 18— 2:50- 4:00 p. m. | 196 | 18 | 2 | |
| Feb. 19—11:00-12:00 a. m. | 206 | 14 | 10 | Fig. 19 |
| 5:00- 6:00 p. m. | 221 | 24 | 12 | Fig. 19 |
| Feb. 20— 4:00- 5:00 p. m. | 244 | No record | | Fig. 20 |
| Feb. 21— 7:00 a. m. | ... | .. | .. | Found dead; autopsy: general peritonitis |

TABLE 3.—*Protocol of Dog O. P. 20*

| Period of Observation | Hours Obstructed | Maximum-Minimum Pressure, Cm. Water | | Notes |
|---------------------------|---------------------|--|---------|--|
| | | Maximum | Minimum | |
| Feb. 16—11:00-12:00 a. m. | .. | .. | .. | Operation; $\frac{1}{4}$ grain morphine; ether; isolated loop in duo- denojejenum; no anasto- mosis |
| 11:00-12:00 p. m. | 12 | 30 | 12 | Fig. 21 |
| Feb. 17—10:00-11:30 a. m. | 24 | 36 | 13 | Figs. 21 and 22 |
| 2:00- 3:00 p. m. | 27 | 44 | 14 | Fig. 22 |
| 5:00 p. m. | 29 | .. | .. | Dead; general peritonitis; per- foration of loop due to apparatus |

TABLE 4.—*Protocol of Dog O. P. 26*

| Period of Observation | Hours Obstructed | Maximum-Minimum Pressure, Cm. Water | | Notes |
|-----------------------------|---------------------|--|---------|--|
| | | Maximum | Minimum | |
| Feb. 27—11:00-12:00 a. m. | .. | .. | .. | Operation; procaine 2%; ob- struction in upper part of jejunum |
| 4:00- 5:30 p. m. | 4 | 17 | 5 | 5 cc. cold water injected into bowel; fig. 4 |
| 9:30-10:30 p. m. | 10 | 8 | 5 | Fig. 5 |
| Feb. 28—10:30 a. m.-1 p. m. | 24 | 36 | 5 | Figs. 5 and 6 |
| 3:45- 4:45 p. m. | 28 | 30 | 6 | Fig. 7 |
| 9:00-10:00 p. m. | 33 | 30 | 6 | Fig. 8 |
| Feb. 29—12:00- 1:00 p. m. | 48 | 28 | 10 | Fig. 8 |
| 3:00- 4:30 p. m. | 51 | 30 | 6 | |
| 8:30- 9:30 p. m. | 57 | 54 | 6 | Fig. 9 |
| March 1—10:00-11:00 a. m. | 71 | 54 | 6 | Fig. 10 |
| 3:00- 4:00 p. m. | 75 | 58 | 6 | Fig. 11 |
| March 2— 7:00 a. m. | .. | .. | .. | Found dead; autopsy showed local adhesions only |

antimesenteric border. In the fourth there was a leak about the apparatus and peritonitis resulted.

In the animals with simple obstruction, perforation or gangrene of the antimesenteric border was not encountered, as in the experiment on animals in which a loop was made. This is of interest, for in the

TABLE 1.—*Data for Dogs Used in Experiment*

| No. | Serial No. | Anesthetic | Site of Obstruction | Duration of Life, Hours | Cause of Death |
|-----|------------|--------------------|---------------------------------|-------------------------|------------------------------------|
| 1 | O.P. 6 | Morphine and ether | Upper part of jejunum | 56+ | Toxemia and general peritonitis |
| 2 | O.P. 8 | Morphine and ether | Lower part of ileum | 78+ | Toxemia and local peritonitis |
| 3 | O.P. 9 | Morphine and ether | Middle small bowel | 102+ | Toxemia and distemper |
| 4 | O.P. 10 | Procaine | Upper part of jejunum | 100+ | Toxemia and local peritonitis |
| 5 | O.P. 11 | Procaine | Middle small bowel | 53+ | Toxemia and local peritonitis |
| 6 | O.P. 12 | Procaine | Lower part of ileum | 77+ | General peritonitis and distemper |
| 7 | O.P. 13 | Morphine and ether | Middle small bowel | 103+ | Toxemia and local peritonitis |
| 8 | O.P. 14 | Morphine and ether | Upper part of jejunum | 76+ | Toxemia and local peritonitis |
| 9 | O.P. 15 | Morphine and ether | Lower part of ileum | 121 | Toxemia and general peritonitis |
| 10 | O.P. 16 | Morphine and ether | Lower part of ileum | 75+ | Toxemia and general peritonitis |
| 11 | O.P. 17 | Morphine and ether | Lower part of ileum | 221+ | Toxemia and general peritonitis |
| 12 | O.P. 18 | Morphine and ether | Middle small bowel | 60 | Toxemia and general peritonitis |
| 13 | O.P. 19 | Morphine and ether | Upper part of jejunum | 130+ | Toxemia and local peritonitis |
| 14 | O.P. 20 | Morphine and ether | Isolated loop in duodenojejunum | 29 | General peritonitis |
| 15 | O.P. 21 | Morphine and ether | Isolated loop in jejunum | 48 | General peritonitis |
| 16 | O.P. 22 | Morphine and ether | Upper part of jejunum | 56 | Toxemia and general peritonitis |
| 17 | O.P. 23 | Morphine and ether | Isolated loop in duodenojejunum | 54+ | General peritonitis |
| 18 | O.P. 24 | Morphine and ether | Isolated loop in duodenojejunum | 45 | General peritonitis |
| 19 | O.P. 25 | Procaine | Lower part of ileum | 29 | General peritonitis (chloroformed) |
| 20 | O.P. 26 | Procaine | Upper part of jejunum | 76+ | Toxemia |
| 21 | O.P. 27 | Procaine | Lower part of ileum | 140+ | Toxemia |
| 22 | O.P. 30 | Morphine and ether | Lower part of ileum | 216 | Chloroformed (fecal fistula) |

latter instance we find that the pressure rose more quickly and reached a higher level, while the sustained pressure between the periods of increased tension was more than twice that found in the animals in which simple obstruction was produced.

Most of the animals, as is shown in table 1, died of a complicating peritonitis. There can be little doubt that this would materially affect the intestinal motility and probably cause the fall in pressure that is

graph was taken within two or three hours of death while the animal was moribund, but it shows what we found the more common record of the intestinal motor activity before death. Without a complicating peritonitis, then, we feel all our graphs would show more evidence of peristalsis than they have done within twenty-four hours of death, but that even without peritonitis the pressure falls and the motility becomes less with the increasing toxemia of obstruction.

Figures 19 and 20 are of interest as they show the changes that come from the development of a fecal fistula. The drainage in this case was not sufficient to empty the obstructed bowel, so that a pressure was kept above the normal but below that within an obstructed bowel without a fistula. A well marked change in the character of the graphs is noted.

SUMMARY

The conclusions that follow from these experiments seem to show that in small dogs with simple obstruction the intra-intestinal pressure is maintained at a level (from 6 to 8 cm. of water) about twice that of the normal maximum (from 2 to 4 cm. of water). While the bowel is active, the pressure rises to ten or fifteen times the normal (from 30 to 60 cm. of water).

What we consider a fairly exact conception of the type and magnitude of the intestinal motility in obstruction throughout its course is shown in the accompanying tracings. Three periods may be roughly distinguished. The first, which embraces the twenty-four hours following obstruction, shows little change from the normal. The second period shows a rise in the basic or sustained pressure with marked peristalsis and a great increase in the intra-intestinal pressure generally. The third or terminal phase shows a falling pressure and a decrease in the peristaltic activity.

The fact that periods of violent peristalsis come on earlier and are more frequent in animals with high obstruction than in those with low obstruction may have some clinical value in helping one to locate the site of obstruction.

In experiments in which an isolated loop was made, the degree of pressure reached (70 cm. of water) is much greater than that in dogs with simple intestinal obstruction.

so marked during the final twenty-four hours. That this is the case might be concluded from the graphs obtained from the animals with high obstruction that are shown in figures from 4 to 11. The last graph was obtained within sixteen hours of death, and the intestinal motility, as is shown by the records, was nearly as active as at any earlier period.

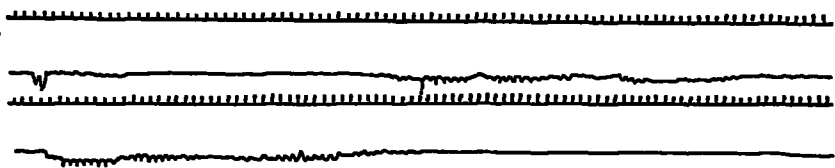


Fig. 20.—Record from animal O. P. 17 after obstruction had been produced for two hundred and forty-four hours; timer 6 seconds.

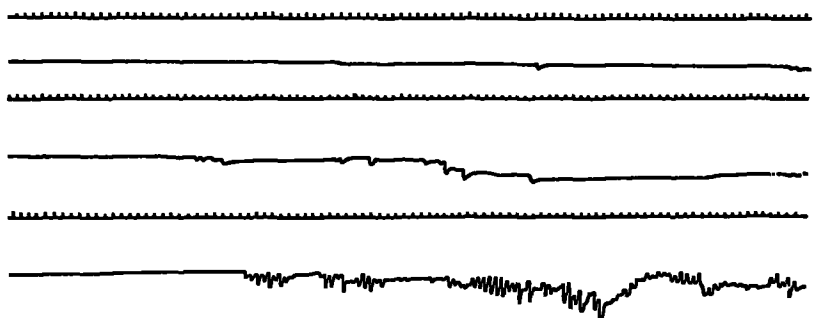


Fig. 21.—The upper two tracings show record from animal O. P. 20 after isolated loop had been produced in the duodenojejenum for twelve hours; the lower tracing, after twenty-three hours; timer 6 seconds.

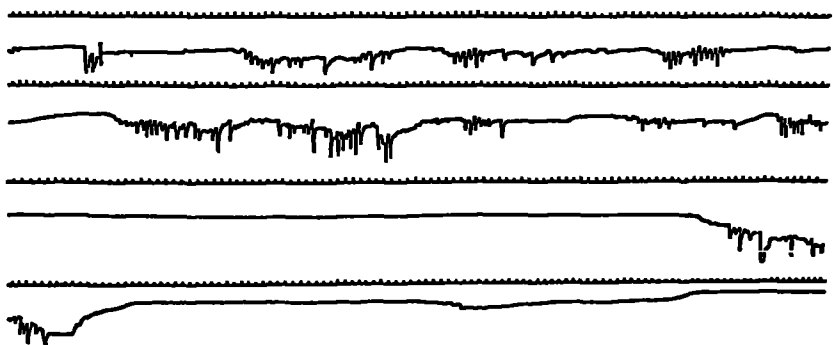


Fig. 22.—The upper two tracings show record from animal O. P. 20 after isolated loop had been produced for twenty-four hours; the lower two tracings, after twenty-seven hours; timer 6 seconds.

Autopsy did not reveal general peritonitis and no local adhesions or exudation beyond what one might expect after such manipulation. Death was thought to be due, therefore, in most part to the toxemia of obstruction. Figure 12 was obtained from another animal with high obstruction that, as shown at autopsy, had general peritonitis. The

rachitic genu varum and valgum represent a regressive phase or variation in the development of growth of the skeleton of the lower extremities. In the new-born child, the knee is in a position of flexion, outward rotation and lateral declination in relation to the general alinement of the leg. Boehm has shown from studies of many children and of anatomic specimens that during the first five years of growth the alinement of the leg changes, the knee rotating slightly inward, losing its flexion and assuming a slight medial declination. However, variations may occur and in certain persons these may be of a regressive type, leading eventually to the formation of genu valgum or varum. Static and mechanical forces resulting from weight bearing were regarded by Boehm as important, not as primary factors in influencing the development of the deformities but as occurring secondarily after the variation in the anatomic development of the leg has been produced.

RICKETS

Historical.—Writing of the history of the knowledge of rickets, Foote³ stated that when Whistler published his thesis in 1645, and Glisson his book in 1650, it was called an entirely new disease. According to present theories of cause, there is no reason to suppose that the disease did not exist before 1650. Swaddling was a method employed by ancient peoples to prevent the development of deformities. Soranus of Ephesus apparently wrote about the disease in the second century A. D. The author has observed in the Army Medical Museum at Washington the skull of a pre-Columbian Peruvian boy with typical rachitic changes. Between 1450 and 1500, Bruges described the disease in England. Portraits by Lochner, Strigal, Bergmaier and others show rachitic changes. Foote concluded that the disease undoubtedly existed at all times and periods.

Sunshine and Skyshine.—Tisdall and Brown⁴ made a study of the effect of seasonal variation on the antirachitic value of sunshine in the latitude of Toronto. Experiments were conducted on albino rats which were kept on a constant rachitogenic diet. The rats were exposed two hours daily and the results appraised from study of roentgenograms and analysis of the calcium and phosphorus in the blood and bone. The authors concluded that the sun's rays in the vicinity of Toronto have slight but definite antirachitic effect, and that there is a sharp increase in the antirachitic effect of sunshine, beginning in March. In April and May, the antirachitic effect is approximately eight times as great as in

3. Foote, J. A.: Evidence of Rickets Prior to 1650, *Am. J. Dis. Child.* **34**: 443 (Sept.) 1927.

4. Tisdall, F. F., and Brown, A.: Seasonal Variation of Antirachitic Effect of Sunshine, *Am. J. Dis. Child.* **34**:721 (Nov.) 1927.

that twice as many rats which had been exposed to the sun survived intraperitoneal infection as those which had not been exposed.

[Ed. NOTE.—The articles summarized reporting the results of investigations of the antirachitic properties of radiation are only a few of a great many dealing with different phases of the same general subject that have been published in the last few years. Little by little the knowledge of the action and effects of radiation is being increased, and already a certain amount of order has emerged from what a short time ago was chaos. While the subject is being approached chiefly from its relation to rickets, the orthopedic surgeon cannot lose sight of the larger bearing of radiation in relation to the function of bone and the treatment of bone diseases in general. It is reasonable to suppose that increase of knowledge concerning radiation in rickets may also have a bearing on the employment of light therapy in other conditions.]

Rachitic Deformities of the Lower Extremities.—Moore⁸ made a study of rickets in the lower extremities. He found that in normal legs the approximating epiphyseal plates of the femur and tibia are parallel and that when the inner borders of the feet are parallel both the knees and the ankles are in contact. In a typical example of rickets, he found that the epiphyseal lines of each knee, if extended, would meet at an acute angle. With the planes of the lower femoral and upper tibial epiphyses coming together on the outside, knockknee would naturally result. The vacant space between the epiphyses in the open part of the angle gradually fills up with calcified bone and new epiphysal planes are formed, parallel to each other but at an abnormal angle to the long axis of the diaphyses of both the tibia and the femur. The author stated that until such a joint becomes fixed in a normal or a valgum or varum position a decided lateral mobility is demonstrable. This exaggerated mobility of the knee is often the first sign of rickets in the leg. A normal knee gives a lateral movement of 3 cm. or less as measured at the heel, regardless of the length of the leg. A knee mobility arthrometer was devised so that mathematically accurate measurements could be obtained each month and become an index of the amount of lateral mobility of the knee. According to the author, this index may be used to determine whether or not genu valgum or varum is imminent. After such a deformity has developed, its value lies in determining whether the joint has become too set to be capable of correction by brace treatment.

DISTURBANCES OF DEVELOPMENT AND GROWTH

The Ovary in Osteomalacia.—Writing on the relation of the ovary to osteomalacia, Fraser⁹ stated that a close relationship between the ovary, pregnancy and osteomalacia has been recognized since Fehling

8. Moore, Ulysses C.: J. Bone & Joint Surg. 10:96 (Jan.) 1928, no. 1.

9. Fraser, J. R.: Am. J. Obst. & Gynec. 14:697 (Dec.) 1927.

December, January and February. These results agree with those of Dorno, who found the ultraviolet content of midday sun in the Alps in January only 10 per cent as great as in July.

Similar methods were employed by the same authors^{4a} in testing out the antirachitic action of skyshine. The rats were exposed on the shady side of the roof. The authors concluded that the effect of skyshine is from about one-half to two-thirds as great as that produced by sunshine.

Hess and Anderson,⁵ by an improved technic, showed that ultraviolet radiation with rays shorter in length than those of sunshine is more potent in healing rickets than the effective area of solar rays. The effective band comprises the waves between 290 and 313 millimicrons. The studies brought out the fact that the area of specific solar radiation is markedly circumscribed, and that a difference of a few millimicrons or millionths of a millimeter determines whether or not waves are effective. During the winter months when the shorter ultraviolet rays do not reach the earth and the longer ones are less intense, the width of the antirachitic zone of sunlight is only about 5 millimicrons. These observations emphasize the danger of the small band of specific radiation being filtered from the atmosphere by moisture, dust, smoke, and other foreign substances.

Tisdall and Brown⁶ tested the antirachitic value of the sun's rays when passed through various special window glasses. These included Vitaglass, Vicray glass and Corning glass. They concluded that the effect obtained was from 25 to 50 per cent of that obtained without the use of glass. An obvious difference could not be detected between the three glasses. The antirachitic effect of sunshine which had passed through ordinary glass was shown to be negligible except immediately adjacent to the window. The authors stated that with any type of glass it is necessary to employ the direct rays of the sun in order to receive much benefit, and that in winter the use of special glass is probably of little benefit.

Robertson⁷ reported an investigation of the effect of exposure to the sun on susceptibility of rachitic rats to infection. The organism used as the infecting agent in the experiments was a gram-negative bacillus isolated from the nose of a normal rat. The author showed

4a. Tisdall, F. F., and Brown, A.: Antirachitic Effect of Skyshine. *Am. J. Dis. Child.* **34**:737 (Nov.) 1927.

5. Hess, Alfred F., and Anderson, William, T.: Antirachitic Activity of Monochromatic and Regional Ultraviolet Radiations, *J. A. M. A.* **89**:1222 (Oct. 8) 1927.

6. Tisdall, F. F., and Brown, A.: Antirachitic Effect of the Sun's Rays Through Various Special Glasses. *Am. J. Dis. Child.* **34**:742 (Nov.) 1927.

7. Robertson, E. C.: *Canad. M. A. J.* **17**:1033 (Sept.) 1927.

do not have blue sclerae do not transmit the disease to their offspring. Little is known concerning treatment, and all present methods are of practically no avail.

Bone Tissue in Conditions of Circulatory Disturbance.—Mueller¹² studied bone tissue from persons with disturbed circulation, such as occurs in arteriosclerosis, and found definite structural changes. The intermediary lamellae showed areas of necrosis, while the lamellar systems surrounding central vessels and marrow spaces were essentially normal. The necrotic areas were found only in the compact bone and were totally lacking in the spongy bone. In senile bone without accompanying arteriosclerosis necrotic areas were not seen. Bone proliferation and evidence of reaction such as are usually seen in the vicinity of necrotic bone areas were not seen in the specimens of bone from patients with circulatory disturbance.

SCOLIOSIS

Lucas¹³ stated that while he considered the treatment of structural scoliosis still far from satisfactory, he had employed Steindler's method with good results. By this method the proper body alinement is maintained by the formation of compensatory curves above and below the primary curve. Direct force is not applied to the primary curve. The first stage of the treatment lasts from one to two months and consists of gymnastics for stretching and loosening the spine and of extension on a Bradford frame. Extension is obtained by applying about 10 pounds to the head and from 30 to 40 pounds to the pelvis. In case there is much deformity of the chest, blowing on Wolff's bottles is prescribed. The second stage is one of fixation and lasts from two to three months. A series of plaster jackets is applied, the child being suspended with the head sling. The arm on the concave side is abducted and the hip on this side adducted. If at the end of this time the body alinement is good, the spine stable with good compensatory curves and the muscles sufficiently strong, the child is sent home in a brace. If the spine is unstable, a fusion operation is performed by Hibbs' method. After operation, the child is kept recumbent for three months with plaster fixation; then a brace is worn for one year longer.

Summarizing an article on scoliosis, Ober and Ghormley¹⁴ stated that functional and mild structural curves can be managed by simple corrective exercises and apparatus. Operative measures are to be recommended in adult patients whose spines are not already fixed by

12. Mueller, W.: Beitr. z. klin. Chir. 138:494, 1926.

13. Lucas, L. S.: Northwest Med. 26:588 (Dec.) 1927.

14. Ober, Frank R., and Ghormley, Ralph K.: Scoliosis, J. A. M. A. 90:361 (Feb. 4) 1928.

introduced castration in 1887. Experimental work has shown that the ovaries exert a marked influence on phosphorus metabolism. Blair Bell mentioned a 50 per cent reduction in excretion of calcium after ovariectomy. Fraser described the changes noted in an ovary removed in midpregnancy from a patient with well marked osteomalacia. Not only the cortex but the entire ovary showed a marked hyperplasia of the glandular and interglandular tissue. There was a general venous congestion and widespread formation of follicles. All stages of maturation of the follicles were seen. Many atretic follicles were present, many of them cystic and with proliferation of the thecal cells. There were more large vessels present than is usually found, particularly in the medulla. This may merely represent a further stage of what normally occurs during pregnancy. The author expressed the belief that the ovary plays a part in osteomalacia because of the therapeutic benefit following castration, the frequent occurrence and aggravation of the disease with pregnancy, the high degree of fertility in this disease, and the changes which the author has described.

Osteogenesis Imperfecta.—Welz and Lieberman¹⁰ reported the occurrence of osteogenesis imperfecta in single ovum twins. The first infant died in nine hours and the second in fourteen hours. The blood calcium in the mother was 8.9 mg. per hundred cubic centimeters of blood, and in the second infant was 10.1 mg. per hundred cubic centimeters of blood. The Wassermann reaction was negative. Roentgen-ray examination of the second infant showed fractures in nearly every bone in both the upper and the lower extremities, in various stages of healing, also healed fractures of most of the ribs on both sides. Marked deformities were present in both femora. There was no evidence of injury to the spine. The clavicles were not broken. The epiphyses of the tibia showed a dense straight line of bone deposit. Roentgen-ray examination of the first infant showed an almost identical appearance. In this case, however, the clavicles were broken.

Brittle Bones and Blue Sclera.—Colby¹¹ reported that there had been brought to his attention three members in one family with brittle bones and blue sclerae. One child had blue sclerae but had not had any fractures. Another child, a girl, aged 5 years, had had four previous fractures from slight trauma. Discussing the disease in general, the author said that it is usually called osteogenesis imperfecta and that it is characterized by brittle bones, blue sclerae, deafness and hypermobility of the joints. It was first described by Von Ammon in 1839. It is transmitted by direct inheritance, and children of affected parents who

10. Welz, W. E., and Lieberman, B. L.: *Am. J. Obst. & Gynec.* 14:49 (July) 1927.

11. Colby, F. G.: *Southwestern Med.* 11:36 (Aug.) 1927.

there is no logical reason for the transmission of pelvic pain into the lower lumbar and sacro-iliac regions.

Etiologic Factors in Sciatic Scoliosis.—That fecal retention in the large bowel may be an etiologic factor in the production of certain disease symptoms, particularly of the syndrome of the so-called sciatic scoliosis, has impressed Osgood¹⁷ from his experience in treating some of these patients. He has made a detailed report of six patients showing this symptom-complex. The duration of the symptoms was very long. All of the usual methods of orthopedic treatment had been tried without avail. Relief was finally obtained from measures directed toward the correction of colonic stasis and fecal retention, such as intestinal massage and colonic irrigations.

Abnormalities of the Lumbar Spine.—O'Reilly¹⁸ continued his investigations of the anatomic abnormalities of the lower spine. He found them present in a high percentage of cases. In a series of 100 roentgenograms, some abnormality was present in 33 per cent, and in an examination of dried bones, abnormalities were found in 17 per cent. The most common abnormality was sacralization of the transverse process of the fifth lumbar vertebra, either fused to the sacrum or articulating with it. The author pointed out the fact that the presence of abnormalities in the so-called normal back frequently leads to legal complications after an injury. In order to prevent this and to protect the workman with a potentially weak back from serious strain, O'Reilly proposed that all workers whose occupations might result in back strain should have a roentgenogram of the spine made before being employed.

Operation for Extra-Articular Fusion of the Sacro-Iliac Joint.—An operation for extra-articular fusion of the sacro-iliac joint was reported by Campbell.¹⁹ The essential feature is the transplantation of a portion of the posterior crest of the ilium into the posterior sacro-iliac fossa and packing it about with bone chips. The postoperative treatment consists of recumbency on a Bradford frame for a period of six weeks. Thus far the author has performed the operation on seven patients. Of these, five are apparently well, and in the other two the operation has been performed too recently to permit an estimation of the result.

[Ed. NOTE.—This operation appears somewhat similar to one originated by Dr. E. G. Brackett about fifteen years ago. He used a transplant from the tibia, while Campbell employed a bone graft from the crest of the ilium. We believe that Brackett has since abandoned his operation in favor of Smith-Petersen's operation.]

17. Osgood, Robert B.: J. Bone & Joint Surg. 9:667 (Oct.) 1927.

18. O'Reilly, Archer: Abnormalities of Lower Part of Back, J. A. M. A. 89: 1128 (Oct. 1) 1927.

19. Campbell, W. C.: Surg. Gynec. Obst. 45:218 (Aug.) 1927.

nature and who are doomed to wear a jacket for life. Fusion operations should not be performed on growing children except in paralytic conditions and then only in case of severe deformity which cannot be held by other measures. In the authors' opinion, the principal indications for operative treatment are: (1) rapid increase of the curve; (2) signs of general debility or ill health; (3) rib pressure with intercostal or pelvic pain, and (4) inability to hold the curve in persons with infantile paralysis. The first three indications are for adults; the fourth is for children or adults.

[ED. NOTE.—We are in agreement with the opinions of the last authors but would supplement their operative indications by adding cases in which the curve is the result of an anatomic defect such as a wedge-shaped dorsal vertebra. Experience indicates that such curves increase with the growth of the patient irrespective of all corrective measures except fusion operations, and sometimes even in spite of them.]

PAIN IN THE BACK

Abdominal Symptoms Associated with Chronic Strain of the Spine.—Carnett¹⁵ expressed the belief that midline abdominal pain may be caused by chronic strain of the lumbar spine and sacro-iliac joints. He observed the condition repeatedly. It is associated with an increased lumbar lordosis and increased dorsal kyphosis. Midline tenderness is found sharply limited to the area of the intra-abdominal portion of the vertebral bodies, and all aspects of the vertebrae and intervertebral disks that are accessible to palpation are uniformly tender. The majority of the patients who exhibit midline tenderness also have an isolated area of tenderness in each iliac fossa over the superior portion of the sacro-iliac joint. The midline tenderness has often been considered aortic tenderness and also sometimes mistaken for tenderness due to appendicitis. In many of the patients with exaggerated lumbar lordosis, the dominant symptoms are those of irritation of the intercostal nerves, which is more or less widespread but is manifested mainly by pain and tenderness over the abdomen, particularly in the right lower quadrant.

Pain in the Lower Part of the Back in Connection with Pelvic Disorders.—The various causes of backache have been considered by Kreuscher,¹⁶ and he has pointed out the infrequency of the production of this symptom by gynecologic disorders. His chief argument against any relationship between uterine conditions and pain in the back is that the innervation of the uterus is derived from the pelvic plexus, the ovarian plexus and a few filaments from the sacral nerves. Consequently,

15. Carnett, John Berton: Ann. Surg. 85:509 (April) 1927.

16. Kreuscher, P. H.: Surg. Gynec. Obst. 45:482 (Oct.) 1927.

important, the author stated, to observe whether the pressure to be relieved is due to the supernumerary rib or to the normal first rib.

The Articular Mechanism of the Diarthroses.—Walmsley²² reported the results of his study of the articular mechanism of the diarthroses. He stated that at the majority of the diarthroses two functions are equally to be served: (1) the function of weight transmission, which is accomplished in only one position and to secure which there are the articular mechanisms, and (2) the function of movement, during which the surfaces of the elements are moved on one another and maintained in their relations to one another by the mechanisms of movement, which are the related muscles. Each function has its own mechanism. Walmsley said that there is one aspect of mechanism of the joints that has not always been taken into account in descriptions of function of the joints and, in fact, is by no means universally admitted, namely, "The definite and nonreciprocal shape of the joint surfaces which determines that they are in full congruence only in the positions in which they transmit weight and are incongruent in all other positions. . . . At the hip joint as the limb moves toward extension, and materially assisted by the anterior inclination of the neck of the femur, the capsule is progressively twisted and shortened, and, as it were, guides the head of the bone like a screw into its socket until at the position of full extension (about fifteen degrees beyond the vertical) the capsule is taut, the head of the bone is screwed home, the surfaces are fully congruent, and further movement of a larger on to a smaller surface is impossible."

[ED. NOTE.—The author brings out a point in reference to the mechanism of the hip that is most important in the reduction of fractures of the hip, namely, the screwing home action of the motion of extension. To approximate the fragments, it is necessary not only widely to abduct and internally rotate the hip, but also to extend it.]

ARTHRITIS

General Articles.—Pemberton²³ stated his conclusions regarding chronic arthritis after a clinical and biochemical investigation of 1,200 cases. He considered the division of the cases into proliferative and degenerative types the simplest and best classification. He thought that the rôle of focal infection in the production of the disease is over-emphasized. He noted evidence of an intimate relationship between arthritis and the nervous system in the frequent occurrence of paresthesia and other vague nervous sensations. In all the large groups so

22. Walmsley, Thomas: *J. Bone & Joint Surg.* 10:40 (Jan.) 1928.

23. Pemberton, Ralph: *Michigan State M. J.* 26:599 (Oct.) 1927.

MECHANICAL DISTURBANCES, ANATOMIC INVESTIGATIONS,
CERVICAL RIBS

Cervical Ribs.—From a study of patients with cervical ribs treated at the Mayo Clinic, Adson and Coffey²⁰ drew the following conclusions: In about 55 per cent of the cases cervical ribs do not cause any symptoms, and patients in whom the condition is discovered purely by accident ought not to be informed of it, as this knowledge is apt to give rise to neuroses with symptoms referable to the rib. The surgical indications depend on the degree and the character of the incapacity produced by the presence of pain, hyperesthesia, anesthesia and circulatory disturbance. Surgical treatment ought not to be advised for the relief of mild, indefinite pain in the neck and shoulder. The authors consider that the anterior approach and tenotomy of the scalenus anticus muscle are preferable to the transcervical approach and resection of the cervical rib, since the same relief is obtained, the procedure is less formidable and postoperative numbness in the arm and palsy of the brachial plexus are avoided.

[ED. NOTE.—It is to be remembered that symptoms apparently due to cervical rib may often be relieved by orthopedic treatment directed toward improving posture and relieving irritation and mechanical disturbances of the cervical spine. Such treatment ought to be given a trial before operation is resorted to. As far as not telling the patient of the accidental discovery of a symptomless cervical rib is concerned, we do not agree with the authors. Leaving aside the ethical question which is here raised, we believe there are few patients injured by the frank discussion of the condition found on examination, provided that the harmlessness of the condition is explained.]

Pressure on the Brachial Plexus by the Normal First Rib.—Brickner²¹ made a study of patients with symptoms of pressure on the brachial plexus caused by a normal first rib. He reported six cases of his own. In the less severe cases the symptoms are pain in the arm, paresthesia and other phenomena. These may be relieved by elevating the shoulder and by exercising the trapezius to keep the shoulder elevated. Three of the author's cases were of this type, the symptoms probably being due to the dragging of the brachial plexus over the first thoracic rib. In the more severe cases all the phenomena of pressure by a cervical rib are produced by the pressure of an abnormal or even a normal first thoracic rib. Several of the patients required operative treatment and were relieved by resection of the first rib. When an operation is performed on a patient with a cervical rib, it is

20. Adson, Alfred W., and Coffey, Jay R.: *Ann. Surg.* 85:839 (June) 1927.

21. Brickner, Walter M.: *Ann. Surg.* 85:858 (June) 1927.

Bacterial infection may have provided the final thrust which started the disease. In the author's opinion, such patients are never cured or the condition arrested by any single line of attack such as removal of foci of infection. Hypertrophic arthritis presents an almost opposite picture. The patients are usually of the thickset type. Bacterial infection is not the cause of the condition, and it cannot be cured by removal of the local foci. Schauffler expressed the view that in the infectious type removal of the foci of infection and the administration of iodoxybenzoate sodium or ammonium intravenously with careful technic is the most efficient treatment in subacute and chronic cases.

Etiology.—Cecil²⁵ discussed the etiology of chronic arthritis. His views may be summarized as follows: In infectious arthritis, the inciting cause is focal infection. The predisposing causes are old age, overweight, faulty posture, occupation, physical defects and exposure. In metabolic arthritis or gout, the exciting cause is uric acid. The predisposing cause is purine diet and heredity.

Jones²⁶ expressed the belief that the lesions in the joints of persons with osteo-arthritis are end-results which may be arrived at by a variety of pathologic states. Quantitative and qualitative alterations, in internal secretions led to disturbances in the normal current of metabolism. It is the opinion of the author that the disease is due to nutritional alterations in the articular structures. They are not inflammatory. Hypothyroidism is common in the disease. Trauma is often the inciting cause. There are two stages in the history of osteo-arthritis. The primary stage is marked by symptoms of villous overgrowth. The later or terminal is the osteo-arthritic phase. Static factors are important. The disease should be recognized in the initial stage. Roentgen-ray examination is usually negative in the early stage.

Relation of Surgical Pathologic Conditions of the Right Lower Quadrant to Chronic Arthritis.—Discussing the relationship of surgical pathologic conditions of the right lower quadrant of the abdomen to chronic arthritis, Taylor²⁷ described the lesions he had been able to demonstrate in patients affected with this disease by roentgen-ray examinations after the patient had ingested an opaque meal. The author's studies and observations are of interest in suggesting the amount of information that may be obtained in regard to the presence and causes of intestinal stasis by thorough work and enthusiastic cooperation between the roentgenologist and the clinician. They point to an association between intestinal conditions and polyarthritis.

25. Cecil, R. L.: *Southern M. J.* 21:20 (Jan.) 1928.

26. Jones, A. B.: *M. J. & Rec.* 126:557 (Nov. 2) 1927.

27. Taylor, Raymond G.: *J. Bone & Joint Surg.* 10:62 (Jan.) 1928.

far studied, women predominated. In the group studied by the author, exposure played an important rôle. Anemia also occurred more frequently in the women who had arthritis. Pemberton's biochemical studies showed that the nitrogenous metabolism is normal in the disease: hence, there is no reason to restrict proteins in the diet. On the other hand, evidence of slowed sugar metabolism has been frequently noted, which the author explained on the basis of poor circulation with less oxygen available for the consumption of the sugar. The blood does not appear to reach the tissues adequately. In a study of the red blood count in arthritis, it was found that the first drop of blood had a lower count than the fourth or fifth, which is the reverse of normal. By studying the capillaries by Lombard's method, the author found them to be less well filled with blood than normal. The capillaries appeared to be contracted. Because of this observation the author experimented with the administration of sodium nitrate in persons with arthritis, but is not yet ready to evaluate the therapeutic efficiency of this measure. The author observed proliferative changes in the patellae of dogs after ligation of the blood vessels to the patella. Pemberton stated that with the exception of removal of foci of infection, vaccines and nonspecific protein therapy, the measures used achieve their effect through their influence on blood flow or metabolism, or both. Arsenic is of value in the treatment of the anemia. Colonic irrigation and colonic massage are sometimes helpful, but in the author's opinion regulation of what is taken into the mouth is of more value. He considered the development of the mechanistic conception of disease and orthopedic treatment based on it a distinct advance. In conclusion, the author attempted to answer the question of what avail is treatment. Of 188 patients who were followed, 24 per cent were completely cured and 73 per cent were definitely improved. He expressed the opinion that most of the present sufferers from arthritis could be saved for a useful life by the methods of treatment now at our command.

Schauffler,²⁴ writing on the subject of chronic arthritis, urged that every physician use some simple method of classification and familiarize himself with the major characteristics of each group in order that he might treat his patients to the best advantage. He has found the most serviceable clinical grouping to be that of Goldthwait: (1) infections; (2) atrophic; (3) hypertrophic arthritis. He stated his belief that the pure infectious type is always due to bacterial infection. The atrophic type is of a different character. The patients are usually of the viscerotrophic type and have always been somewhat delicate. There is usually a history of worry, overwork or mental shock, and there is evidence of disturbed body chemistry or of endocrine imbalance.

24. Schauffler, Robert M.: Arthritis, J. A. M. A. 89:1748 (Nov. 19) 1927.

only from 2 to 3 per cent. In a series of 107 cases, the distribution according to sex was males, 97; females, 10. Thomas believed that the precipitating factor is not infrequently trauma, either directly to the joint or indirectly in the form of ill advised or careless urethral instrumentation and treatment, excessive activity or sexual excitement during the acute stage of the urethritis. The arthritic symptoms usually manifest themselves during the second or third week; the earliest case recorded is five days. However, involvement of the joints may supervene at any time throughout the acute or chronic course of the disease or in the presence of urethral or uterine adnexal complications. In Thomas' experience, the symptoms have been polyarticular in 58 per cent and monarticular in 42 per cent. The joints have been involved in the following order of frequency: knee, 58 cases; hip, 50; wrist, 21; shoulder, 19; phalangeal, 17; elbow, 13; metatarsophalangeal, 8; spine, 8; metacarpophalangeal, 7; sacro-iliac, 1; temporomaxillary, 1, and sternoclavicular, 1. In respect to treatment, Thomas called attention to what he believes is a current mistake on the part of the orthopedic surgeon and the genito-urinary surgeon; namely, that they center too much on the treatment of the joint or the prostate or the seminal vesicles as the foci of infection, with apparent lack of appreciation of the fact that the condition is a septicemia. Thomas felt that the first step should be to treat the blood stream infection either by biologic therapy or by chemotherapy; second, to eradicate the focus or foci of infection in the genito-urinary tract, and third, to treat the involved joint or joints by local methods.

(To be Continued)

Smith²⁸ expressed the belief that intestinal stasis is responsible for many cases of polyarthritis, and that in certain cases surgical intervention to relieve the cause of it is required. However, this should never involve resection or sidetracking of the involved portion of the intestine. He also believed that implantation of *Bacillus acidophilus* in the cecum is helpful in certain cases.

[Ed. NOTE.—Surgeons were at one time enthusiastic in the attempt to relieve persons with intestinal stasis by operations. Numerous operations were performed in different disease conditions, including arthritis. The results were disappointing, and the radical method of treatment has been generally abandoned. Smith obtained some interesting results, and his work is suggestive and should be continued. Its chief value at present, however, is again to call attention to the importance of the intestinal factor in the treatment of persons with arthritis. The present armamentarium of the physician is varied and large enough to deal with this condition without resorting to operation.]

Treatment of Arthritis with O-Iodoxybenzoic Acid.—Of twenty-one patients with chronic arthritis who were treated with salts of o-iodoxybenzoic acid, Cottrell²⁹ found that all but three showed improvement. The relief of pain was often prompt and marked. In the majority of chronic cases, there was an improvement of function from a slight to a marked degree. In the author's opinion the drug is best given in courses of from six to eight doses semiweekly, with from three to six weeks' rest between each course. Intravenous administration is the method of choice, although the drug may be given orally in capsule form. The latter may be followed by nausea.

Gout.—According to Harbison,³⁰ gout is probably often overlooked. All parts of the body should be examined for tophi. It should be remembered that in this condition bursae often become inflamed. The diagnosis is made by examination of the tophi. The author places considerable reliance on the determination of blood uric acid and advises that this examination be made in every patient with obscure pains in the joints. A blood uric acid content of more than 5 mg. is suggestive of gout. Other conditions in which the blood uric acid may be high are leukemia, polycythemia, interstitial nephritis and febrile states. The treatment is dietary, with purines eliminated. The protein may be high. Colchicum is still the best drug to use.

Gonorrheal Arthritis.—Thomas³¹ wrote that the incidence of arthritis as a metastatic complication of gonorrhea is not great, averaging

28. Smith, R. M.: *J. Bone & Joint Surg.* 10:57 (Jan., 1928).

29. Cottrell, J. E.: *Am. J. M. Sc.* 174:523 (Nov., 1927).

30. Harbison, J. E.: *Gonorrhea & Ven. Dis.* 27:352 (Sept., 1927).

31. Thomas, E. A.: *Gonorrheal Arthritis*, *J. A. M. A.* 89:2174 (Dec. 24, 1927).

at that time, which is composed only of the identical tissues that are in a state of active hyperplasia in the normal parts of the same breast.

(a) *At Birth and Puberty.*—My conclusions are based on examinations of the breasts of children (male and female) who were born dead; of those who were in the years immediately preceding puberty and of those who were at the age of puberty. The deaths of many of the children whose breasts were examined occurred at full time and were due to traumatic causes; the conditions of their breasts could not possibly

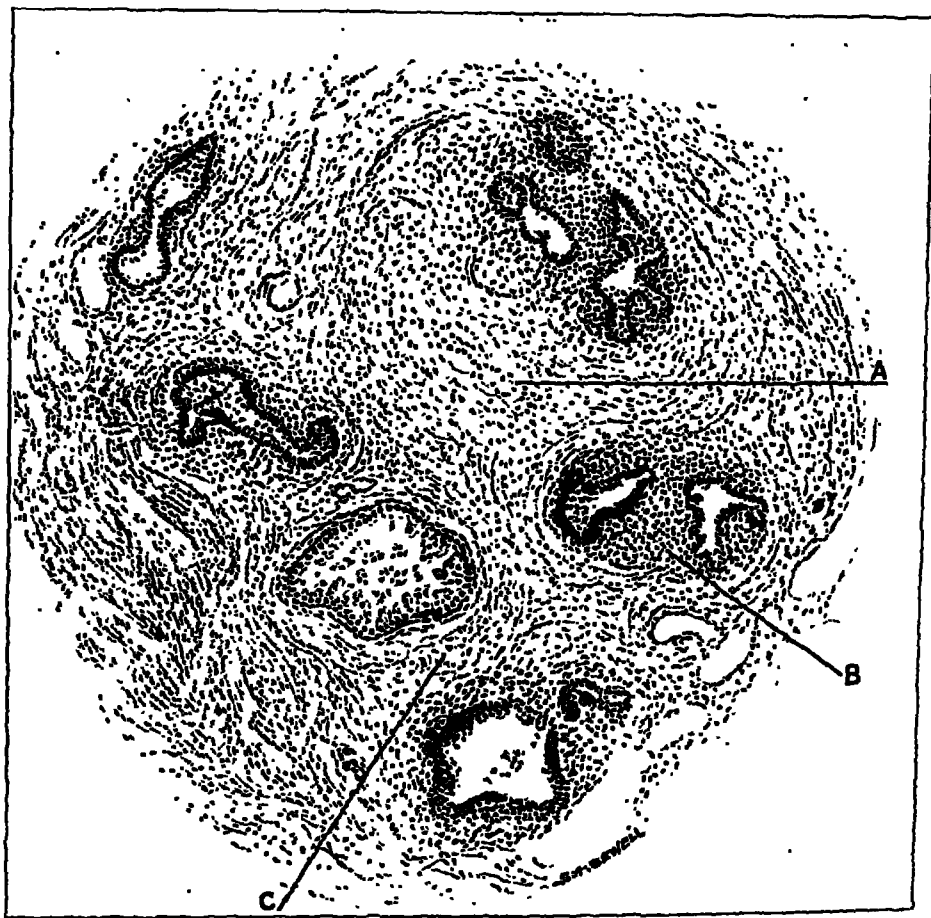


Fig. 1.—Microscopic appearance of part of a male breast at birth—full term. The death was caused by a rupture of the tentorium during birth. At A, B and C, the pericanalicular and periacinous connective tissue is in a state of hyperplasia among the fibers of which lymphocytes have accumulated. There is desquamative epithelial hyperplasia in the acini and terminal ducts. There is no elastica in this breast. Compare with figure 2.

be assigned to antenatal disease. The morphologic appearances I describe are those of normal active changes and are present in varying degrees in all breasts at birth and at puberty.

It is impossible to distinguish between male and female breasts at birth, but the subsequent changes, at puberty, for example, are more marked in females; therefore, I shall describe only female breasts in

"CHRONIC MASTITIS," "CYSTO-ADENOMA" AND ADENOMA OF THE BREAST

G. LENTHAL CHEATLE, F.R.C.S.

LONDON, ENGLAND

In writing this paper, I have had several objects in view. The first object is to place the so-called "chronic mastitis" in its correct etiologic and pathologic position. Its morphologic appearances are identical with those of the physiologic active state at birth, at puberty and in certain phases of lactation (fig. 1). This active state becomes pathologic (fig. 2) when it is present at from about 30 to 45 years of age and induces diffuse pain, and when fibro-adenomas (usually of the same type as those which form at puberty) develop in its occupied areas (figs. 3 and 4). These two separate occurrences belong to the condition to which the term "chronic mastitis" is so universally applied.

A second object is to point out that the commonest type (fig. 6) of fibro-adenoma that occurs at puberty is a local exaggeration of the physiologic and active hyperplasias which are normal at puberty. A third object is to point out the importance of a state-of formations of epithelial tumors in the ducts and acini—which crops up in the literature. of a pathologic condition in several guises and disguises, including that of "cysto-adenoma." A fourth object is to describe a true adenoma of the breast.

ETIOLOGY AND PATHOLOGY OF CHRONIC MASTITIS

In this part of my paper I shall describe (a) the similarity between the normal active morphologic appearances present in the breasts at birth, at puberty and in lactation;¹ (b) the etiologic connection between the activity of the breasts at birth, at puberty and in certain phases of lactation, and the morphologic appearances which are now commonly associated with the term chronic mastitis, and (c) the etiologic association that exists between the general active changes of the breast at puberty and the formation of the commonest type of fibro-adenoma that arises

1. While writing the results of my investigations, my attention was called to some of the contents of an article by John Fraser (Surg. Gynec. Obst. 45:246 [Sept.] 1927). I am glad to see that he shares my conviction that the best method of examining breasts is to cut whole sections of the glands—a practice which I have adopted and taught for thirty years. I cut the whole sections in paraffin, not in celloidin.

these periods. The changes occur mainly in the terminal ducts and acini, and concern hyperplasia of the epithelial, pericanalicular and periacinous connective tissue.

At birth, the epithelial hyperplasia may be one of two kinds, one type being desquamative and the other formative or genetic. That one type may sometimes be more obvious than the other depends on the stage reached in development. The desquamative type belongs to the



Fig. 4.—Microscopic appearance of the fibro-adenoma *B* in figure 3.

later stage. I will not refer to the formative type here; I may say, however, that these genetic morphologic appearances are like the more dangerous states of dysgenetic epithelium which are seen in pathologic glands in later life.

In the desquamative type of epithelial hyperplasia at birth, to which I now refer, the ducts and acini of the whole breast are filled by small, irregularly shaped, badly staining epithelial cells which have been cast off and are incapable of further life. Also, around the ducts and acini of the whole breast there is an extensive hyperplasia of rather loosely constructed pericanalicular and periacinous connective tissue among the



Fig. 2.—Photomicrograph of part of a whole section of breast removed from a married woman, aged 38, who had three children, the youngest being 8 years old. Extreme pain in this breast had been borne for eight or ten years. The photograph has been taken at the posterior margin of the breast *D*. At *D* there is a slight undulation which would not be appreciated by digital palpation. *B* points to a lobule in which there is hyperplasia of the pericanalicular and periacinous connective tissue among the fibers of which lymphocytes have accumulated. In the terminal duct *A* there is a desquamative epithelial hyperplasia (type a) which can be seen in the acini. The epithelial hyperplasia is distending these structures. There was no discharge from the nipple. Compare with figure 1.

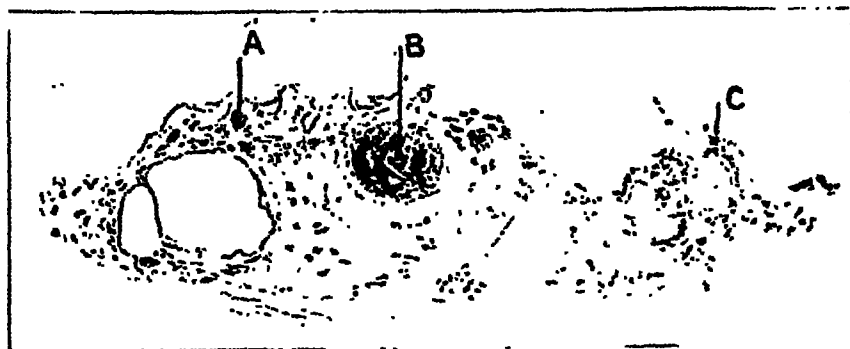


Fig. 3.—Microscopic appearance of section of whole breast which was removed subcutaneously from a married woman, aged 42. Multiple cysts and pain were the cause of its removal. In the more dense looking parts of the section, there were the same signs as those seen in figures 1 and 2. In addition, at *A*, *B* and *C* there were fibro-adenomas in various stages of formation, of which *B* is the most advanced. They belong to the type of the usual fibro-adenoma which occurs at puberty.

complain of diffuse pain in their breasts. The morphologic appearances in these breasts are those on which the supposed manifestations of inflammation are based. They cannot be regarded as being inflammatory any more than can the same active normal signs which are present at birth and puberty.

Paradoxical as it may seem, "chronic mastitis" is really a physiologic process which has become pathologic by being present when it should be absent, by developing an excess of desquamative epithelial hyperplasia which induces pain by distention (fig. 2 *A*) and by possessing the same liability as the breast at puberty to form fibro-adenomas which may or may not develop acini within their formations of tumor (figs. 3

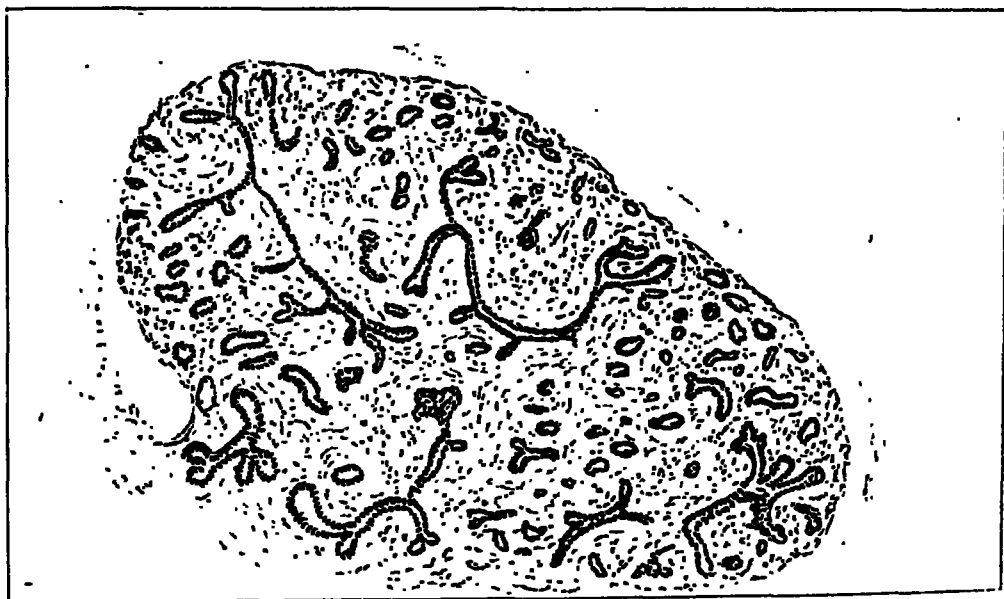


Fig. 6.—Microscopic appearance of a small fibro-adenoma taken from *B* in figure 5. It is the usual type of fibro-adenoma that occurs at puberty and shows the dense hyperplasia of the periacinous and pericanalicular connective tissue.

and 4). For some inexplicable reason, the breasts of some women at any age between 30 and 45 exhibit the state seen at birth and at puberty.

A new and more descriptive name than chronic mastitis is wanted; in my previous communications on the subject I have described it under the heading of "Desquamative Epithelial Hyperplasia type A." I do not look on it as a dangerous state, and it may remain uncomplicated by another pathologic process.

Clinicians are apt to describe these breasts as being nodular all over their anterior surfaces. The posterior surfaces, which are clinically inaccessible, are smooth (fig. 2 *D*). The anterior surfaces of these breasts, and of most breasts of women at this period of life, are presumed to be nodular, for the following reason: As the glands become

fibers of which lymphocytes are present (fig. 1). These appearances are constant, and I regard them as part of a normal physiologic process of development.

This enormous activity ceases in the years between birth and puberty and after lactation. After birth and before puberty, the desquamative epithelial hyperplasia ceases; there is often almost a complete atrophy of the pericanalicular and periacinous tissue, and the connective tissue that is more obvious than any other is the ordinary supporting connective tissue of the breast.

At puberty the whole condition seen at birth recurs in more regular and less rampant formation, and lymphocytes also reappear among the increased and actively reforming pericanalicular and periacinous con-

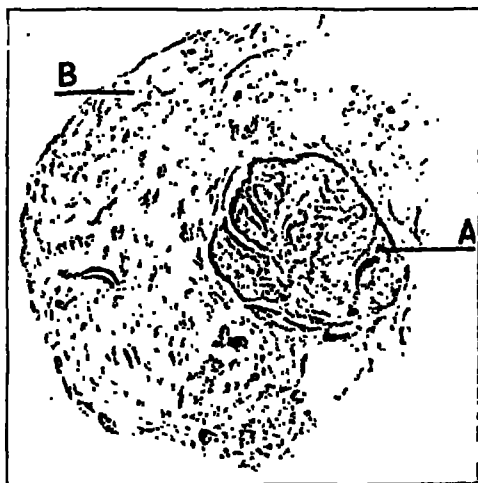
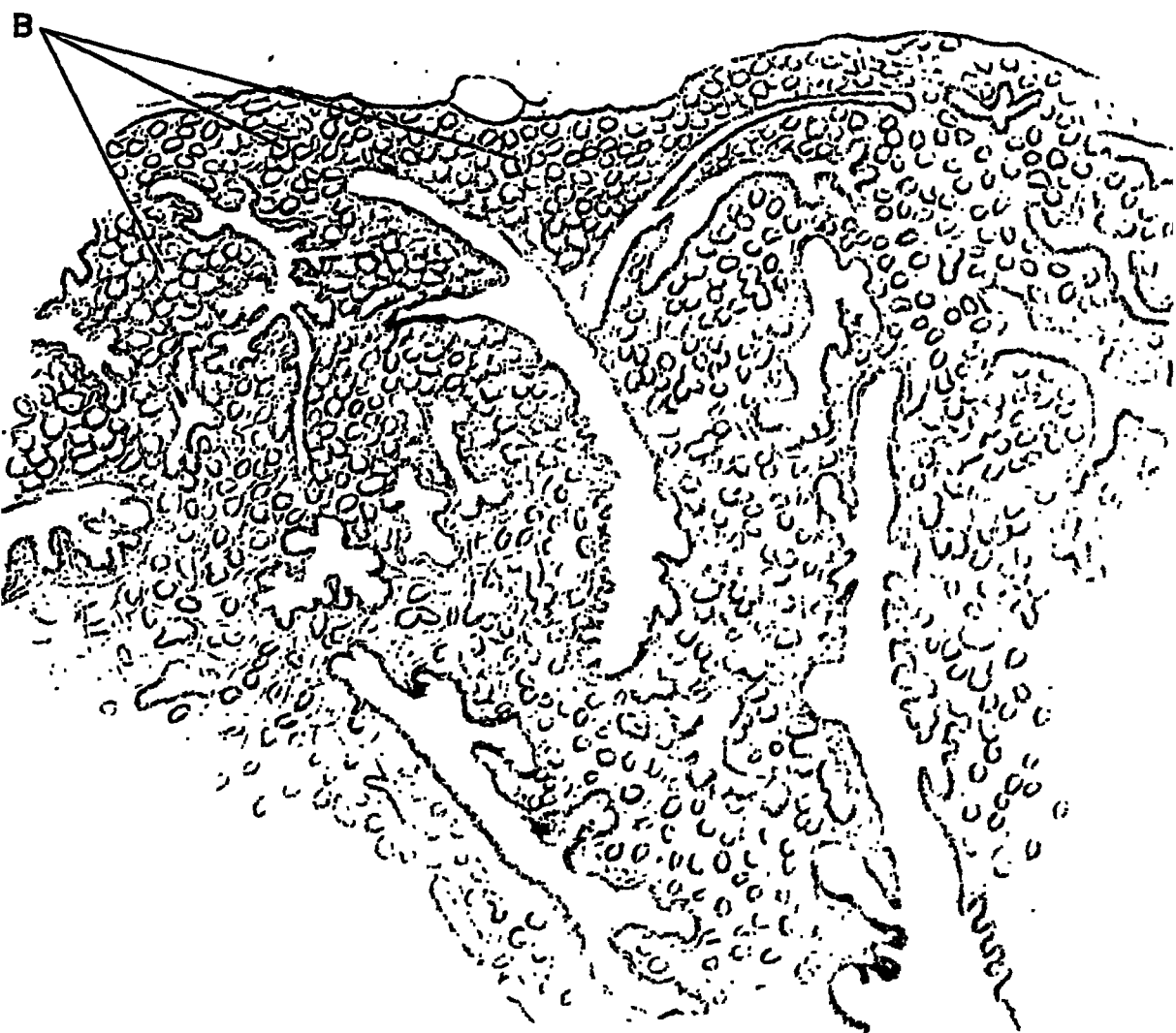


Fig. 5.—Microscopic appearance of a segment of breast removed from a married woman, aged 22, who had noticed the lump *A* for four years. *A* is a fibro-adenoma belonging to the type that usually occurs at puberty. Figure 6 shows *B* in this figure. On the edge of the tumor at *A* there has been an enormous increase of normal looking acini (see fig. 7 *B*).

nective tissue. New acini form and take their part in the enlargement of the breast. After puberty, there is again a great deal of atrophy of the acini and also of the pericanalicular and periacinous connective tissue and a cessation of desquamative epithelial hyperplasia. The appearances of this latent state may remain more or less constant throughout life if lactation does not occur. I now pass on to the merging of these normal changes into pathologic states.

(*b*) *Etiologic and Morphologic Appearances.*—In the first pathologic state, namely, the so-called “chronic mastitis,” the morphologic appearances in the epithelium and pericanalicular and periacinous connective tissues are identical with the active states I have described in breasts at birth and at puberty (compare fig. 2 with fig. 1). They are seen between the ages of 30 and 45 in many women and in a few men who



J. E. REVELL

A

Fig. 7.—Microscopic appearance of section taken from the edge *A* of the tumor in figure 5. At *B* there is an enormous increase in the number of acini which do not differ in appearance from those in the rest of the section. The duct *a* has been stained, and it has undergone a slight irregular hyperplasia around the ducts of the tumor.

former, instead of being comparatively loose, is much more dense and compact than in the rest of the breast and affects only a segment of the breast. The size of the segment affected differs in various tumors. The epithelial changes are also those of desquamative epithelial hyperplasia. In some of these tumors of puberty there is also an enormous

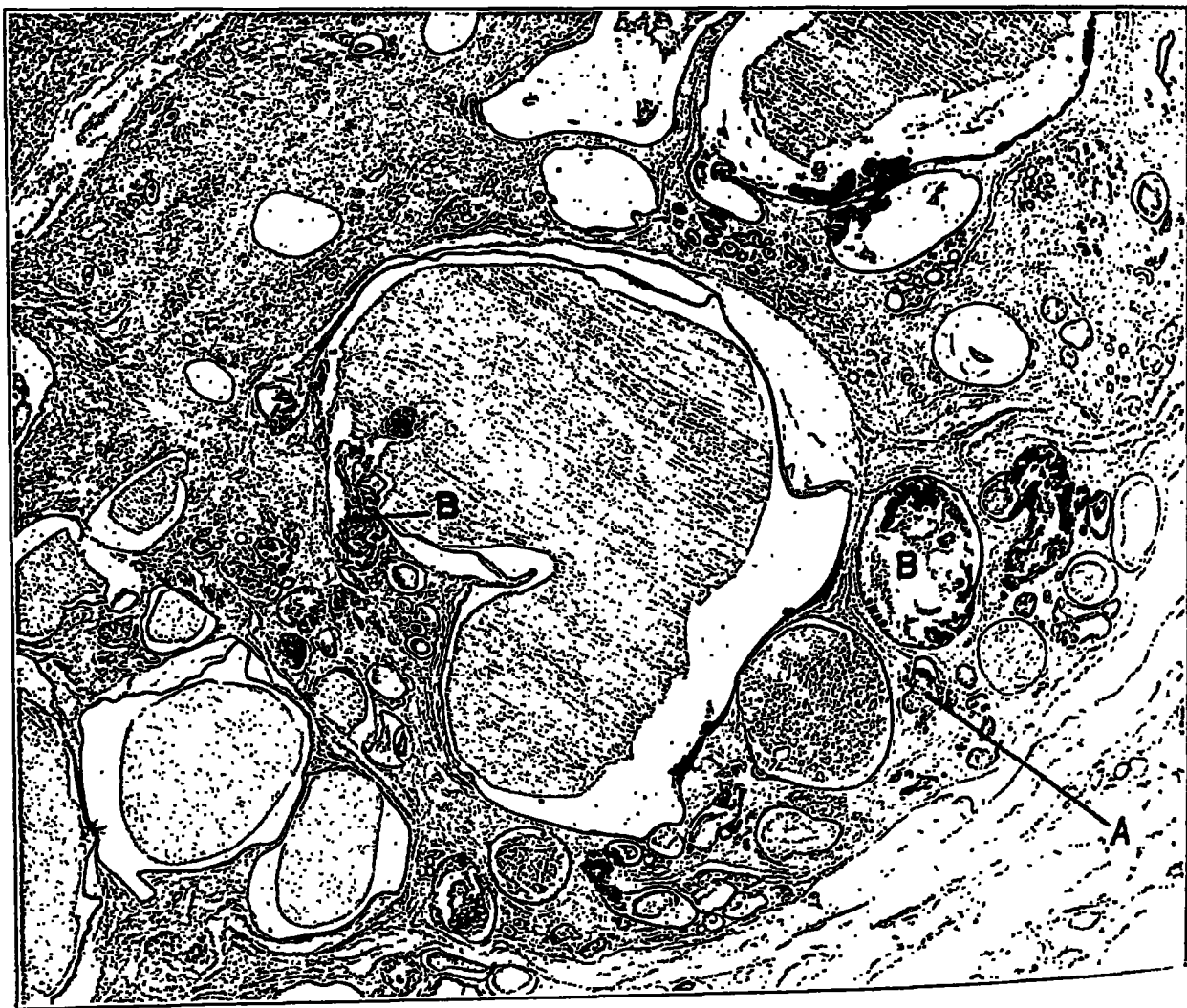


Fig. 9.—Photomicrograph taken from figure 8. *B* and *B* is a dilated duct containing papillomatous and sessile dysgenetic epithelial hyperplasia. At *A* there is a collection of acini which are distended by the same type of sessile epithelial growth.

development of acini (fig. 7) which further accentuates a perverted likeness to the physiologic hyperplasia that is occurring in the rest of the breast at puberty. I particularly wish to point out that this tumor commonly begins at puberty and originates in the same tissues that are normally active at puberty. The whole tumor may be regarded as being a more or less localized perversion of a normal physiologic state.

pendulous, and especially after lactation, the ligamenta suspensoria of Sir Astley Cooper become thickened. The thickened branches as they approach the skin to which they are attached include fat lobules which are so isolated in the process that they appear as separate nodules. If the skin of these breasts is undercut the cutaneous attachments of these ligaments are divided, and the underlying structures then feel smooth, and nodularity is not found.

(c) *Etiologic Association Between Active Changes in Breast and Fibro-Adenoma.*—The second pathologic condition to which I refer is the etiologic connection that exists between the active (figs. 5, 6 and 7)

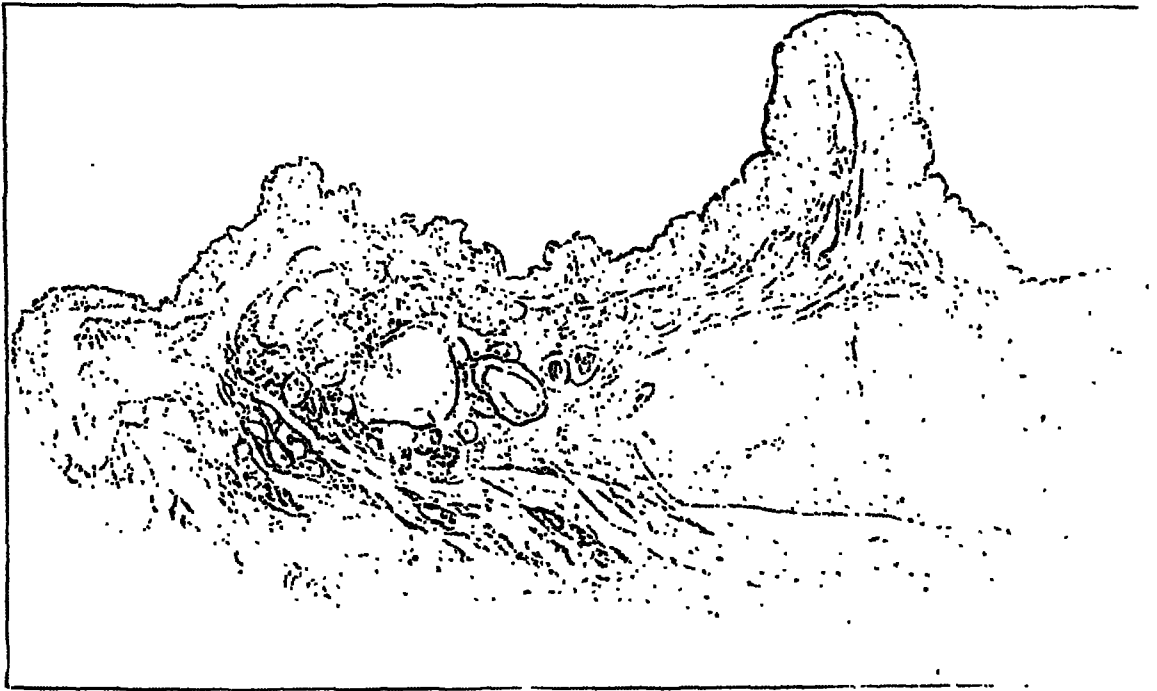


Fig. 8.—Photomicrograph of whole horizontal section of breast from a married woman, aged 36. Removed for the presence of the localized painful nodularity due to the lesion seen on the left of the section. The affected duct and its branches can be seen to be dilated from the prominent nipple in the center of the section to the periphery where there are comparatively large cysts which contain dys-genetic epithelial hyperplasia seen at A and B of figure 9 and at A and B of figure 10. Carcinoma is not present in this breast. There was no discharge of any kind from the nipple.

changes at puberty and the formation of that type of fibro-adenoma which is the most common one at that time. Precisely the same tissues which form this tumor are actively undergoing normal hyperplasia in other parts of the breast at the same time; the pathologic difference between the fibro-adenoma and the rest of the breast is that the hyperplasia of the pericanalicular and periacinous connective tissue in the

must be negligible when compared with the new glandular formation that occurs in the adenoma described in the latter part of the paper; (2) that it is commonly composed of a series of separate tumors—papillomas and sessile epithelial growths in preexisting ducts and acini—

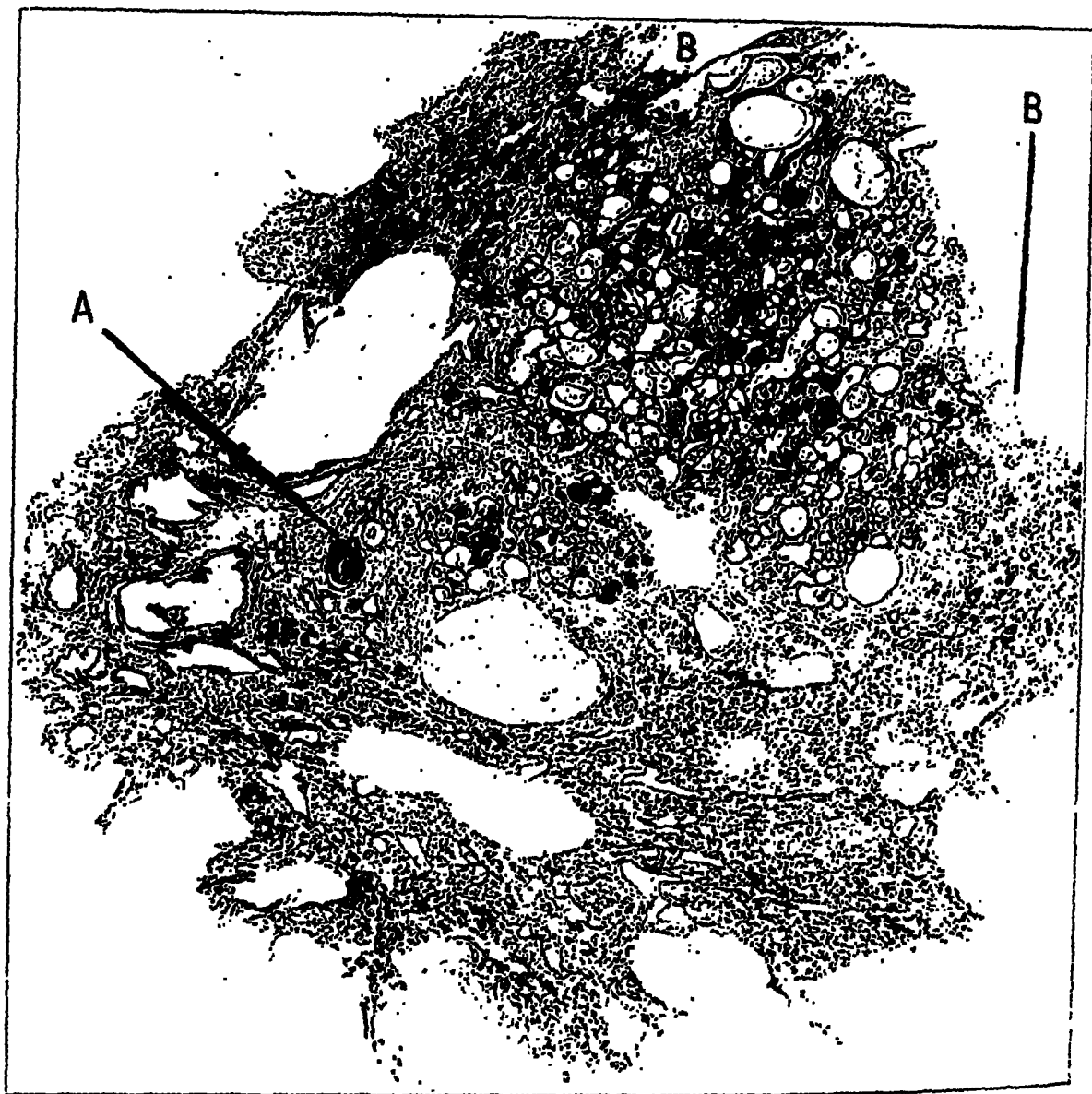


Fig. 11.—Photomicrograph of whole section of breast in which are all the morphologic appearances seen in figures 8, 9 and 10. The section was made vertically in order to show the triangular form of the state described in the text. *A* points to the apex of the triangle in front of which the nipple was situated. The lines *BB* point to the limits of the base of the triangle. The lesion was in the depths of the breast. Palpation revealed only a density in its area of occupation. Carcinoma is not present in this breast. There was no discharge of any kind from the nipple.

Recognition of the fact that there is an etiologic connection between the pathologic changes I have mentioned and physiologic activity makes a clear and comprehensible point from which to begin consideration of all problems related to the incidence and genesis of pathologic (dys-genetic) hyperplasia.

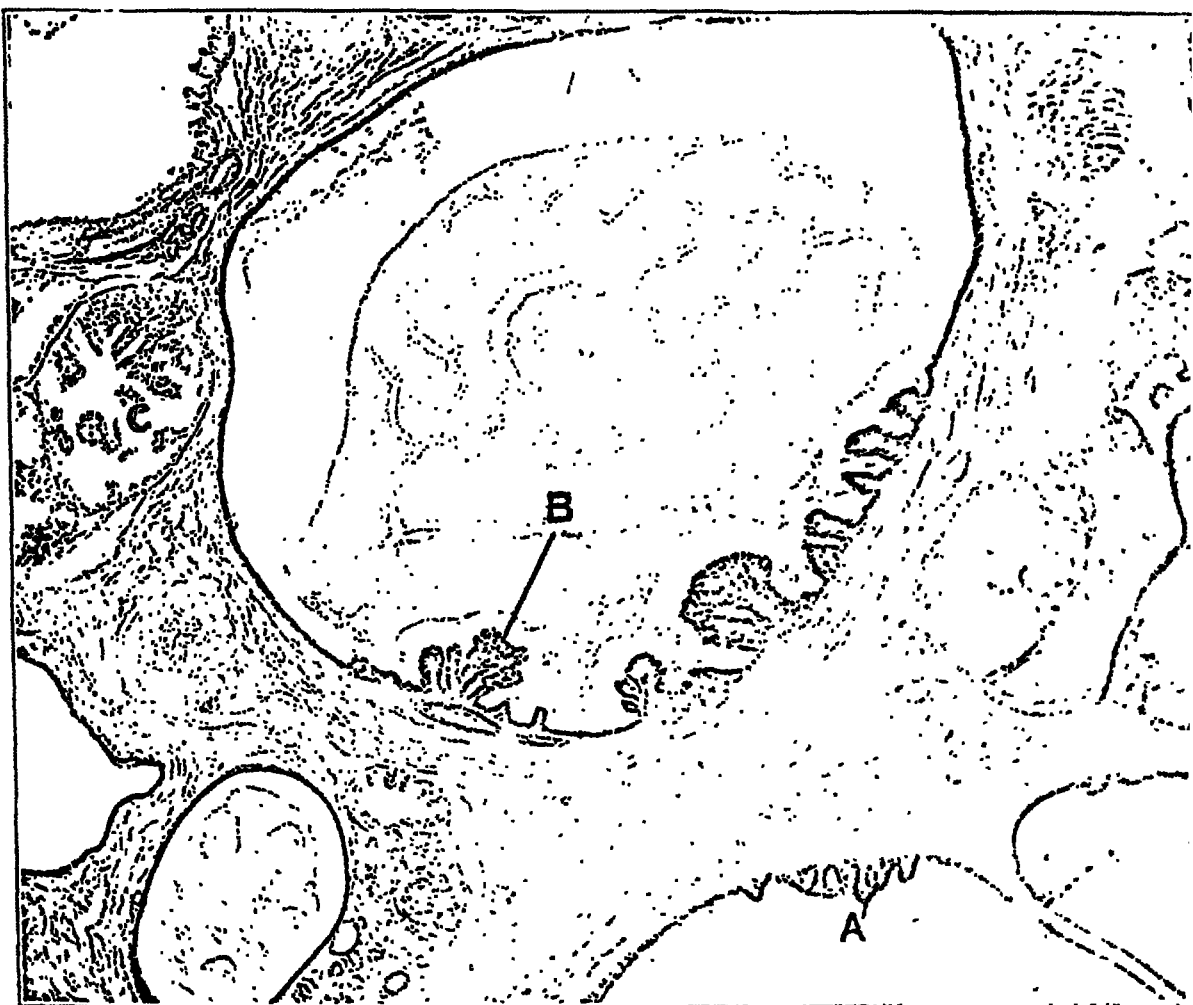


Fig. 10.—Photomicrograph taken from figure 8. In the dilated duct A and the small isolated origins of multiradicular papillomas can be seen. The epithelial layer covering the tips of some of the stalks has already joined with that covering the tips of stalks in juxtaposition to each other. Alveolar spaces lined with epithelium are formed in this way. In the dilated acini C, the epithelial hyperplasia is passing from the desquamative to the dys-genetic type.

DESCRIPTION OF CYSTO-ADENOMA

My object in this part of the paper is to describe the tumor that is now termed "cysto-adenoma" and to point out that it is not to be considered that there is any new formation of acini, and that it is not

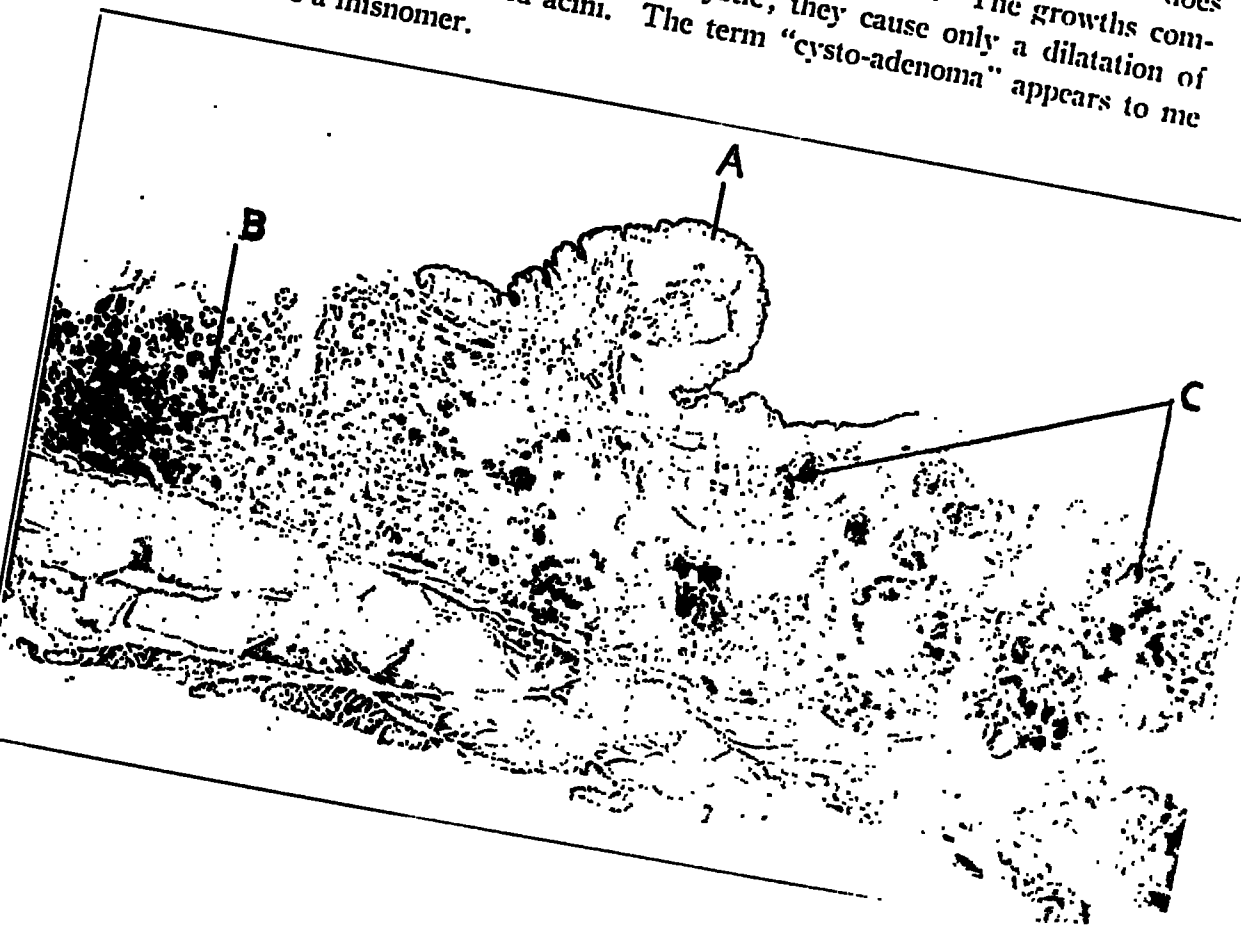
cysto-adenoma of the breast has no more right to the term than the multiple adenomatous papillomas of the colon, which the changes in cysto-adenoma of the breast so closely resemble. No one suggests calling the condition in the colon cysto-adenoma. The origin of the term as applied to the breast can be explained in the following way: The ducts of the breast are not of large caliber like the tube of the



Fig. 13.—Photomicrograph taken from upper and central parts of the lesion C in figure 12. The ducts are full mainly of papillomas, and the dilated acini are distended by a sessile epithelial hyperplasia. They are more obvious around the margins of this section. *A* marks the spot in which the carcinoma had begun (see fig. 14).

colon; they are tubes of small caliber which become convoluted and distended and when cut in sections for microscopic examination look like separate cysts, whereas they really are parts of convoluted tubes in perfect continuity. It is important to know all about this state, because it

and greatly resembles the condition of multiple adenomatous papillomas in the large intestine.² In the breast, the epithelial hyperplasia may be more sessile than papillomatous and vice versa; (3) that it is usually a much more diffuse condition than it is generally supposed to be: (4) that it is as full of danger to the patient as the multiple adenomatous papillomas of the colon, and (5) that the term "cysto-adenoma" does not convey correctly the actual state of the tumor. The growths composing the state do not become cystic; they cause only a dilatation of preexisting ducts and acini. The term "cysto-adenoma" appears to me to be a misnomer.



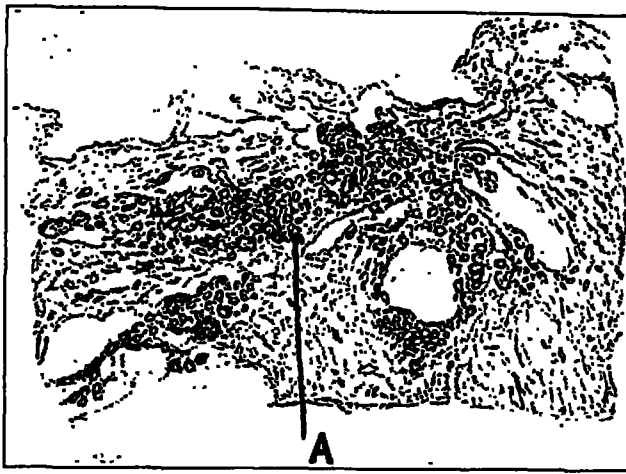


Fig. 15.—Part of a whole section of a breast removed from a married woman, aged 44. Removed for pain which corresponded in situation to an area of density. There was no discharge of any kind from the nipple. The epithelial hyperplasia was papillomatous in the ducts to a much less degree than in the breasts shown in figures 8, 11 and 12, and was much more sessile in character. There is early carcinoma in this breast at *A*, shown in figure 16. The axillary lymphatic glands were not affected.

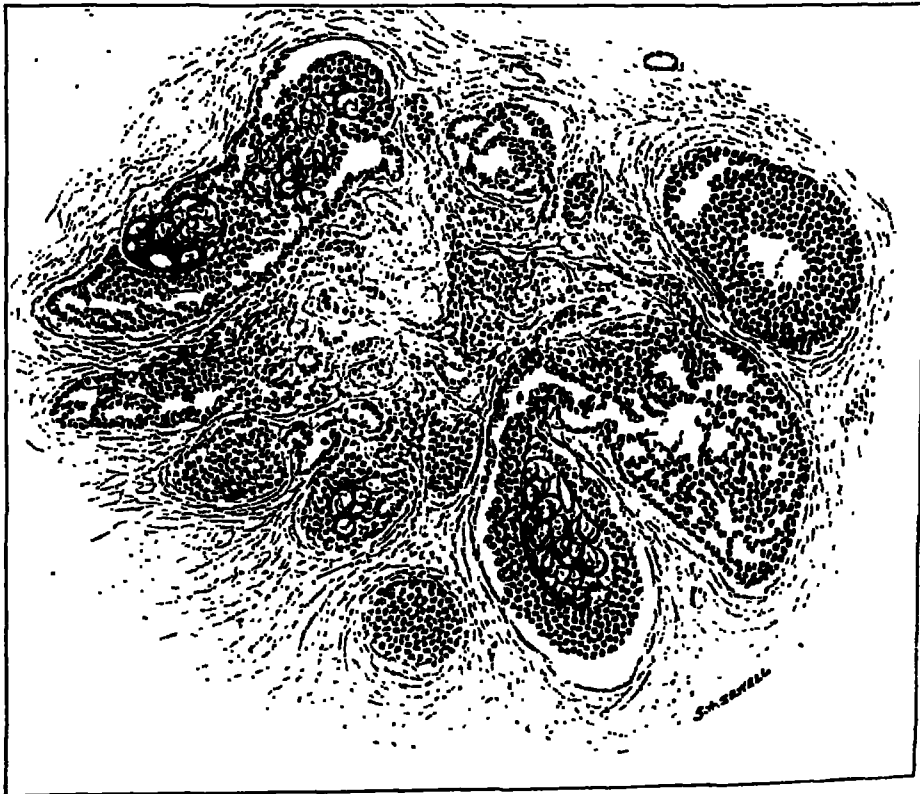


Fig. 16.—Drawing of *A* in figure 15 under higher magnification showing terminal ducts and acini filled with a sessile dysgenetic epithelial hyperplasia. In two of the terminal ducts, it has undergone colloid degeneration. Some epithelial cells have escaped and are invading the connective tissue of the breast.

is often regarded rather casually as being free from danger, whereas, in reality, it is so pregnant with probable danger in all instances and with positive danger in some that when it appears most benign it should be regarded as closely allied to carcinoma as the multiple adenomatous papillomas of the colon. On the other hand it is sometimes described, in exaggerated examples, as being carcinoma, when in reality all the



is not present in these breasts. In figures 12, 13, 14, 15, 16 and 17, the distribution of the disease is affecting precisely the same regions. In figure 16, taken from figure 15, and in figure 14, taken from figure 12, there is undoubted carcinoma which has spread among the supporting connective tissue of the breasts and has not affected the fat outside the breast nor the axillary lymphatic glands. The same state may be seen in the ducts and acini of figure 17. In this specimen the carcinoma has invaded the connective tissue of the breast, has undergone colloid degeneration and has spread to one lymphatic gland in the axilla.

When carcinoma does not originate purely in the terminal ducts but when its acini also contain the original malignant epithelial hyperplasia, the state can be seen without exception in every early case of carcinoma of the breast, and sometimes it can be demonstrated—if the elastica is particularly stained—in late cases of carcinoma when nearly

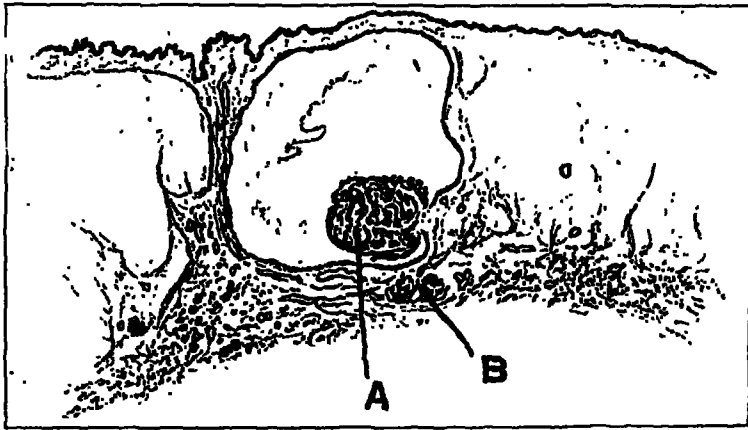


Fig. 18.—Drawing of a whole section made from the breast of a married woman, aged 56. There is a large dilated duct, on the right of the nipple, in which there is a tumor (*A*) with a papillomatous attachment to its wall. The continuation of the duct is also dilated and contains papillomatous and sessile epithelial hyperplasia (*B*). There was no discharge of any kind from the nipple. The tumors were benign.

all the morphologic evidence of its site of origin has been lost in the chaos of growth and spread. Lastly, it is an important and dangerous state on account of its clinical obscurity when it exists in the substance of the breast, both when carcinoma has not begun and also when carcinoma is present in its earliest stages. If the condition appears in a duct the distribution of which is on the surface of the gland, and when there is only a thin layer of fat between it and the skin, as shown in figures 8 and 12, its presence can be detected by a localized triangular nodularity with the base toward the periphery of the gland (figs. 11 and 17). I cannot exaggerate the importance of local nodularity as a clinical sign. When it affects a surface diet and when the layer of fat

the complete distribution of the epithelial growth can be seen to be diffuse in the affected ducts much more often than is generally supposed. With the aid of these large sections and also with that of certain clinical features, I will next point out the importance and danger of the subject. Later, I will describe the nature of the epithelial hyperplasia.



as it traverses the gland to reach the periphery and a short branch directed backward to reach the posterior surface of the gland. Throughout the courses of ducts, lobules of acini are connected to them by smaller ducts. During lactation, the nipple is crammed with acini and is distended to so great an extent that morphologically they appear to be the main constituents of the nipple. After lactation, they disappear completely.



Fig. 20.—Tumors *B* situated lower down in the same duct *A* of figure 18. The papillomas have undergone the same development into glandular reproductions of less typical character compared with *A* in figures 18 and 19.

The epithelial hyperplasia of this so-called "cysto-adenoma" may exist only in the duct as it passes through the nipple or only in the ampulla of a duct, or it may exist only in the main branch before it divides (figs. 18 and 21). On the other hand, it may extend throughout the whole course of a duct from the ampulla to its periphery and involve the acini to such an extent that they all contain some form of

between it and the skin is thick, its clinical signs on palpation resemble the same condition when it is in the substance of the gland. In both these instances it appears as a localized lesion, harder than the rest of the gland and incapable of further diagnosis by palpation. Pain that usually accompanies this state is always referred to this denser area of the breast. There may also be a history of an intermittent discharge of



ous even than the purely papillomatous type. In the ducts the epithelial hyperplasia behaves a little differently from that in the acini. It may affect the duct in two ways. First, it may be papillomatous. When the tumor is of this type it arises in a multiradicular manner from many stalks of fibrous tissue which are usually composed of the whole wall of the duct, and the elastica can be stained in their centers (figs. 10 *A* and *B*); or, less commonly, it may arise from the intra-elastica connective tissue, when there is no elastica in the stalks. However papillomas arise, they are always covered by the columnar epithelium of the duct. The papillomas arising from the intra-elastica do not branch so freely as those which contain the elastica; they remain small, and epithelium piles itself on the top of them. The papillomas containing the



Fig. 22.—Photomicrograph of whole section of breast removed from a married woman, aged 48. The main part of the epithelial hyperplasia is confined within the boundaries of normal ducts and has a decided papillomatous arrangement of less orderly character than that in figures 18, 19, 20 and 21. At the lower left part of the periphery of the tumor, epithelial cells have invaded the connective tissue. There was no discharge of any kind from the nipple, and the axillary lymphatic glands were not affected.

elastica may undergo various changes. They may appear as small growths, but usually they branch extensively and the epithelium on the tips of their branches coalesces with branches of the parent papilloma and with those of contiguous stalks to form alveoli lined by epithelium (figs. 10 *A* and *B*). A papilloma may more rarely develop into an arrangement which constitutes a small mammary gland or adenoma containing ducts and acini (figs. 18 and 21). When this process occurs,

the dysgenetic epithelial hyperplasia. I have a specimen—presented to me for examination by Mr. Sampson Handley—in which the whole lengths of two ducts and their acini are involved in this manner. Again, only one of the main branches may be thus affected throughout its course (figs. 8, 11, 12, 13, 15 and 17) or even a few or only one of its terminal branches and acini may contain the epithelial hyperplasia. There are no clinical signs on which a limited distribution can be diagnosed from an extensive one, and no one can tell from clinical signs whether he is dealing with a growth only in the ampulla or



tain a carcinoma; for example, it is hard to believe that all the epithelial changes seen in *A*, in figures 22 and 23, in which carcinoma is present, did not begin in this way, and it is probable that the advanced carcinoma in figure 24 is an advanced tumor which had the same origin. Accompanying the papillomatous tumors there is generally a sessile epithelial hyperplasia without any fibrous stalks, which may completely fill a portion of a duct. Sessile and papillomatous formations are commonly seen together when long branches of ducts are affected. Sometimes the sessile epithelial hyperplasia is more in evidence than the papillomatous. If that is so, the state is more dangerous than if it were chiefly papil-



Fig. 24.—Photomicrograph of whole breast removed from a married woman, aged 36. There was no discharge of blood from the nipple. Lymphatic glands in the axilla contained carcinoma. The patient died of the disease eight months after the radical operation. The extension of this carcinoma was one of the most rapid and diffuse the author has seen. The appearances suggested a papillomatous arrangement, and the epithelial cells were columnar. The three tumors depicted in figures 18, 19, 20 and 21 appear to be benign examples of a state which may pass on to the malignant condition seen in figures 22, 23 and 24.

lomatous. For instance, when only a terminal duct and its acini are affected, the epithelial hyperplasia may be only sessile in the ducts and acini. The acinous papillomas are not so common, and when they occur they are composed of fine fibrillous stalks which do not branch

it usually takes place in the main duct. It is interesting to observe that all the epithelial and glandular elements of this particular intracanalicular tumor (figs. 19 and 20) are derived from the columnar cells which originally lined the duct.



distended boundaries. The changes may exist in a breast in which carcinoma is not present. There are examples in which at some place or other the epithelial cells have invaded outside structures and unsuspected carcinoma is present (figs. 2, 13, 14, 15 and 16). It is difficult to discover the focus of exit of these invading cells, even after examination of sections carefully cut in series.

PURE ADENOMA OF THE BREAST

My object in this part of the paper is to describe the purest type of adenoma I have observed in the breast. It is a rare and benign



Fig. 26.—A representative part of the adenoma *A* in figure 25.

tumor. On the one hand, it differs from the cysto-adenoma by a massive new formation of pathologic adenomatous elements—a new formation of ducts and acini does not occur in cysto-adenoma. On the other hand, the pure adenoma differs from a fibro-adenoma, in which a new formation of ducts and acini may occur (fig. 7), by a complete absence of the dense hyperplasia of the pericanalicular and periacinous connective tissue which is characteristic of fibro-adenoma (fig. 6). The pure adenoma resembles the cysto-adenoma by exhibiting papillomatous and sessile epithelial hyperplasia which dilates the structures in which it grows. The feature which distinguishes the pure adenoma from all

At the operation, the tumor was as large as the girl's fist. Enlarged lymphatic glands were not found in the axilla, and the girl was well two years after the operation.

The second example of this type was a tumor removed from a married woman, aged 34, who had three children. The microscopic appearance of this tumor is shown in figure 27. The tumor consisted of a massive new formation of pathologic adenomatous elements chiefly composed of dilated acini. They may lie in juxtaposition or they may be separated from each other by loose connective tissue. The epithelial elements may consist of a simple layer of cuboidal shaped cells. The cells may pile themselves on the top of one another to form columns three or four cells in height, and the epithelial cells may grow on delicate fibrillous stalks to form papillomas which do not branch. Collections of cells may be sessile (fig. 27).

Clinically, the tumor was growing. The exact pathologic state was not clear at the operation, and the gland was removed as for carcinoma. Microscopic examinations proved that none of the axillary lymphatic glands was affected. The patient was well twenty years after the operation.

other tumors of the breast is that it consists only of a massive new pathologic formation of ducts and acini. The new formation of ducts (fig. 25) may be more excessive than the new formation of acini (fig. 27) and vice versa. I do not know whether this tumor can become malignant. I have seen only two examples. One was a tumor and part of a breast from a girl, aged 15 years (fig. 25). The tumor was composed of a massive new formation of pathologic adenomatous elements in which formation of new ducts predominated. Within the ducts papillomas had grown (fig. 26). The elastica was continued from the



organism into animals has produced lesions in the colons of rabbits and dogs in all essentials like those found in man. Thus, the disease has been established as an infection of the colon, and for want of a better term the original designation of chronic ulcerative colitis or colitis gravis has been retained.

The infection of the colon is severe and carries with it serious complications and sequelae, such as polyposis, perforation, stricture, hemorrhage, perirectal fistula and abscess, endocarditis, splenomegaly, mesenteric thrombosis, ocular phenomena, tetany, severe anemia, arthritis and malignant disease. The malignant condition, although not common, is undoubtedly the one most dreaded.

In the records of the Mayo Clinic from 1916 to 1927, inclusive, I noted reports of twenty-three cases of chronic ulcerative colitis in which it was believed, because of various clinical and pathologic signs and symptoms, that a malignant disease of the colon had developed. Post-mortem examination in three of these cases failed to reveal malignant disease. There was, instead, extensive ulceration and polyposis. In three others the proof was large filling defects in the colon, with sudden and rapid change of symptoms, obstruction, cachexia and anemia. A specimen for diagnosis was not obtained. In the remaining seventeen cases the condition was proved to be malignant, either by the specimen removed or at necropsy.

I shall include in my discussion, therefore, twenty cases of malignant disease, the seventeen in which the condition was proved by examination of tissue and the three in which it was proved by clinical diagnosis. The age incidence in these cases is significant. Whereas five patients had attained the age of 50 or more, the other fifteen were between 21 and 45 (three were aged 21, 23 and 26 years, respectively; six were between 30 and 39; six were between 40 and 45). Only one patient (a woman, aged 53) gave a history of malignant disease in the family: two uncles had had carcinoma. Nineteen patients were white; one was a mulatto. Fourteen patients were farmers; one was a laborer, one a railroad conductor, one a lawyer, one the wife of a physician, and two were bookkeepers. Symptoms of chronic ulcerative colitis were complained of for from three months to thirty-five years before admission. Only one patient had had symptoms for thirty-five years; the average duration of symptoms of the other nineteen was six years.

The medical treatment had varied, as is usual in these cases. In a few cases, injections of vaccine had been given subcutaneously; in most of them, rectal irrigations with one or another of the so-called intestinal antiseptics had been given.

In most of the cases, a fairly definite change of symptoms could be elicited by which the beginning of the malignant process could be esti-

REPORT OF ILLUSTRATIVE CASES

CASE 1.—A boy, aged 9 years, first came to the Mayo Clinic in 1915. He had suffered with diarrhea for a year or longer, and was passing from five to six stools a day which contained much blood, mucus and pus. As he lived only twenty miles from Rochester, he visited the clinic during the following ten years whenever the trouble became severe, which was several times each year. On his first visit he was placed on treatment for amebiasis, which consisted of emetine, hydrochloride, administered hypodermically, and irrigations of coal-oil. Repeated examinations of the stools did not reveal amebas or parasites of any kind. A diagnosis of colitis was made proctoscopically. Every cold caused an exacerbation of the colitis, and the patient had colds and tonsillitis at all seasons of the



Fig. 1 (case 1).—Roentgenographic appearance of the colon after a barium enema in 1924.

year. Finally, in July, 1924, he was brought to the clinic in an exhausted condition with severe bronchitis and had to be taken to the hospital at once. At this time he said that as long as he could remember he had never passed fewer than six or eight stools in twenty-four hours and that they were always mixed with blood. For weeks after he had a cold, he passed from fifteen to twenty-five stools in twenty-four hours, with severe cramps and tenesmus before and during each passage.

Successive examinations of the stools for endamebas and acid-fast bacilli again gave negative results, but by culture of the scrapings from the bases of the ulcers many gram-positive diplococci were found. The patient had a low grade fever and the maximal leukocyte count was 19,300. The proctoscope revealed active ulcerative colitis, graded 4. Roentgenograms of the colon showed that it was shortened and tubelike (fig. 1). The patient had the pasty appearance of a

CASE 2.—A man, aged 26, came to the Mayo Clinic on Oct. 2, 1925. He said that about ten years previously he began to have bloody purulent rectal discharges with frequent watery stools. At first this occurred at intervals with remissions. In 1917, he was well enough to be admitted to the army, although he did not tell the members of the examining board of bowel trouble. While in the army he spent most of his time in the hospital, a severe exacerbation having occurred in 1917. He passed from twenty to twenty-five bloody stools daily, many of them at night. He had been discharged from the army partially disabled and was well until 1922. From then until his admission into the clinic, diarrhea had been continuous, and his vitality was low. During these years, an average of from six to eight stools was passed a day. He had lost 15 pounds (6.8 Kg.) in the last two years; his weight on admission was 128 pounds (58.1 Kg.).



Fig. 3 (case 1).—Same section as that shown in figure 2; $\times 340$.

Pus and blood were found in excess in the stools. Parasites, ova and acid-fast bacilli were not found. The culture yielded the usual diplococcus. On October 2, the hemoglobin was 45 per cent; erythrocytes numbered 3,680,000. The tonsils were septic, and three teeth contained periapical abscesses. Perirectal excoriation, a draining fistula on the right and an anorectal stricture, which barely admitted the index finger, were present. The Wassermann reaction of the blood and the urinalysis were negative. Roentgenograms of the chest, kidneys, ureters and bladder were negative. Roentgenograms of the colon showed narrowing and shortening but no haustra (fig. 4). Proctoscopic examination disclosed a granular ulcerative process, resembling a polyp, and a stricture from 2 to 3 cm. from the anus.

Treatment consisted of a filtrate of the diplococcus, administered subcutaneously, tincture of iodine, 12 minims (0.74 cc.) three times a day, and instillations of witch-hazel daily. The patient improved steadily, and on October 24,

pain was relieved by bowel movement. Two years previously the diarrhea became more severe, and there was more blood and pus; for about six months before admission the pain had been more constant, and the patient had lost 32 pounds (14.2 Kg.). From six to fifteen stools were passed in twenty-four hours. The more he ate the worse the pain became.

After a thorough investigation, a diagnosis of chronic ulcerative colitis was made, and the "Brown operation" and appendectomy were performed. The ileum was severed completely, and the proximal loop only brought out. The patient returned in 1919 much improved, having gained 30 pounds (13.6 Kg.), but he considered the ileostomy opening a nuisance because the prolapse kept him from working. A no. 1 ring pessary was inserted, which seemed to control the prolapse.



Fig. 5 (case 2).—Section of one of the many hyperplastic islets of mucosa disseminated throughout the colon and removed at necropsy; $\times 75$.

In February, 1920, the proctoscopic examination showed a stricture 5 cm. above the anus, so small that the lumen could not be seen. The mucosa showed that the colitis was still active, although the patient was clinically in a fair condition.

The patient secured a job as a taxi driver and supervised his farm. He returned in 1925 in good physical condition, weighing 178 pounds (80.7 Kg.). The stricture in the rectum would not admit the index finger. The ileostomy opening with the aid of the pessary was functioning well. He returned home and was in fair health until about the middle of September, 1927, when the sanguinopurulent rectal discharge increased greatly and at the same time a dull, aching, steady pain

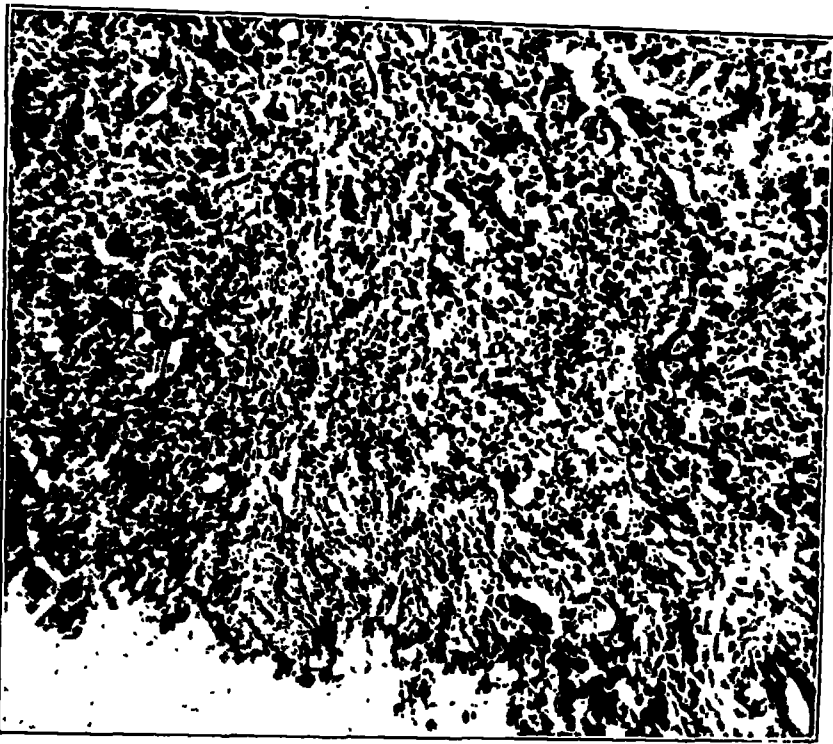


Fig. 7 (case 3).—Section of one of the numerous nodular excrescences of the rectal mucosa removed for diagnosis; $\times 150$.

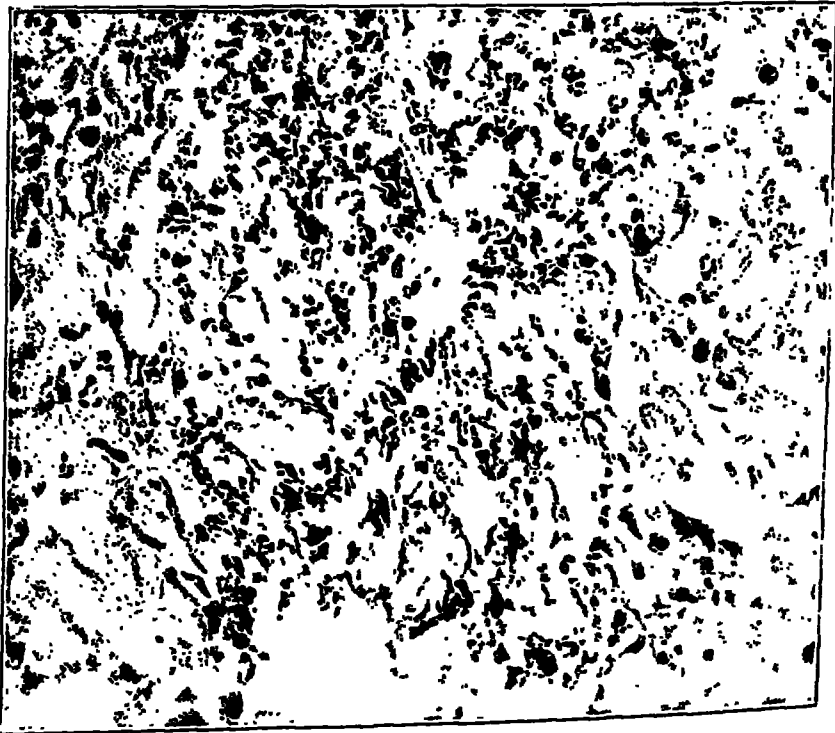


Fig. 8 (case 3).—Same section as that shown in figure 7; $\times 340$.

developed at the lower end of the rectum. This became severe in a few days and persisted until his admission to the clinic on December 15. He complained of shooting pains in the genital region, frequency of urination and much difficulty in voiding.

The patient was now 51 years of age. He weighed 158 pounds (71.7 Kg.). The facial appearance was of one in distress. The leukocytes numbered 12,400, and polymorphonuclears, 79 per cent. Proctoscopic examination under regional anesthesia showed the rectal surface to be covered with a grayish, foul-smelling slough, with many irregular areas protruding here and there as far as could be seen. Proctoscopy could not be carried further than 14 cm., because of the limitation of motion and narrowing of the lumen. A specimen of one of the many irregular

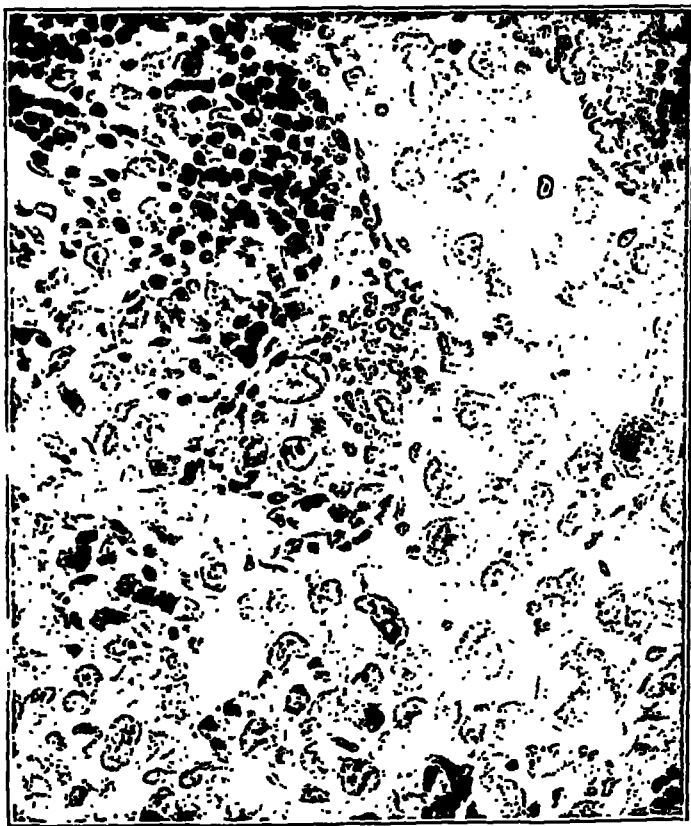


Fig. 6 (case 2).—Same section as that shown in figure 5; $\times 325$.

nodules proved to be adenocarcinoma, graded 3 (figs. 7 and 8). The first phalanx of the index finger was inserted into the rectum, and the mucosa felt rough and stiff. The patient is receiving radium treatment elsewhere.

CASE 4.—A youth, aged 19, first came to the Mayo Clinic on June 28, 1916. He had been passing loose, watery stools containing flecks of blood for nine years. Proctoscopic examination showed granular proctitis. A roentgenogram of the colon was negative. The hemoglobin was 76 per cent. On his return to the clinic on August 21, roentgen-ray examination showed the colon to be thickened and contracted. Achlorhydria was present. From 1916 to 1920, he got along fairly well, with the exception of periods of frequency of urination, the urine containing blood and mucus. In the first ten years of his trouble, he had had several

patient died on September 20. On this day the blood urea was 252 mg. for each hundred cubic centimeters. Necropsy revealed carcinoma of the transverse colon (figs. 10 and 11), metastasis, chronic ulcerative colitis, generalized peritonitis and multiple infarcts in the lungs. The ulcerative colitis was not active, the mucosa being smooth and shiny, with a suggestion of many healed scars.

CASE 5.—A man, aged 40, came to the Mayo Clinic on Feb. 26, 1923, because of diarrhea of sudden onset two years previously. The rectal discharges averaged from three to fifteen every twenty-four hours. The stools were soft and were mixed with blood and mucus. There was considerable flatulence, and some tenesmus and cramps preceding each bowel movement. The diarrhea was more severe in the afternoon and at night. An acute cold in January had made the diarrhea much worse.



Fig. 10 (case 4).—Section of the tumor which was removed at necropsy and which corresponded to the filling defect shown in the roentgenogram; $\times 75$.

At examination, the Wassermann reaction of the blood and the urinalysis were negative. The leukocytes numbered 10,700. Three teeth with periapical infection and somewhat enlarged tonsils were noted. A roentgenogram of the chest was negative. A roentgenogram showed the colon to be smooth and without haustra. Proctoscopic examination showed rather mild activity in the colon, with greater activity in the sigmoid. Parasites or ova were not found in the stools. A diagnosis of chronic ulcerative colitis was made. Tincture of iodine was given by mouth, and a mild solution of protargin and witch-hazel were given by rectum. On March 26, proctoscopic examination did not show improvement. The patient was dismissed, and the condition of the bowels continued as before until Dec. 20, 1926, when, following the lifting of a heavy grain sack, excruciating pain appeared in the right lower quadrant. This continued for two weeks, during which the patient was disabled. The temperature was taken and found to be between 99

hemorrhages and became anemic. Intermittent distress at the umbilicus was relieved by bowel movement. He did better on a full diet. In 1920, he had had influenza, after which the condition became somewhat worse. In 1924, the distress increased and bowel movements were more frequent. After a trip south in April, 1927, the urgency and frequency of bowel movements increased, and he went to Battle Creek Sanitarium where he was placed on a vegetable and fruit diet. After this, emetine and stovarsol had been given, but without improvement. In June, the pains became so severe that he "couldn't get his breath." The pain was worse after a bowel movement; morphine was given for relief. On June 24, a hemorrhage from the bowel occurred. His physician wrote to the clinic for some vaccine which was given during August; blood was believed to have disappeared from the stools after this.



Fig. 9 (case 4).—Roentgenographic appearance of the colon in 1927 showing the typical deformity of chronic ulcerative colitis and a definite filling defect in the transverse colon.

At examination, September 7, the hemoglobin was 60 per cent, the erythrocytes numbered 4,600,000, and the leukocytes, 6,100. The chief complaint was that of intermittent severe attacks of pain in the upper part of the abdomen which was relieved by morphine, of which he had as much as 3 grains (0.195 Gm.) daily. Proctoscopic examination showed chronic ulcerative colitis, graded 2. A roentgenogram of the colon after an enema of barium showed ulcerative colitis of the entire colon with a filling defect from a constriction of the transverse colon (fig. 9). The urine showed hyaline casts, graded 4, and pus, graded 1.

On September 9, ileostomy was performed for carcinoma of the transverse colon and metastasis to the pelvis. After a stormy postoperative course, the

every twenty-four hours. Between April 7 and 11, five deep muscular injections of immune horse serum¹² were given, that is, 10, 15, 15, 15 and 15 cc. were given on successive days. After this, the temperature receded and after April 12 did not go above 99 F. The patient improved gradually and was dismissed on April 17, weighing 113 pounds (51.3 Kg.). He was advised to take the filtrate prepared



Fig. 12 (case 5).—Specimen removed surgically.

from the diplococcus every four or five days, and kaolin if he needed it. At this time he was having from four to six daily bowel movements without blood. On June 6, he had gained 16 pounds (7.3 Kg.), was having three or four daily bowel

12. Rosenow, E. C., and Bargen, J. A.: Unpublished data.

and 101 F. He returned on Jan. 5, 1927. A tender, firm, nodular mass in the right lower quadrant was fairly adherent to the structures around it. Proctoscopic examination at this time showed typical chronic ulcerative colitis, graded 2. The roentgenogram showed that the bowel did not contain haustra, but there was a filling defect in the cecum. The tonsils and infected teeth had not been removed. *Trichomonas hominis* was found in the stools. A culture from the ulcers in the bowel yielded the usual diplococcus. The hemoglobin was 57 per cent, and the leukocytes numbered 12,100. The patient had lost 17 pounds (7.7 Kg.) in a few weeks.

On January 13, ileocolostomy was performed for a cecal tumor which appeared malignant and was surrounded by inflammatory tissue. The adjoining glands were enlarged. Following a fairly uneventful convalescence, four deep exposures of roentgen rays were given as part of the treatment. The patient was dismissed

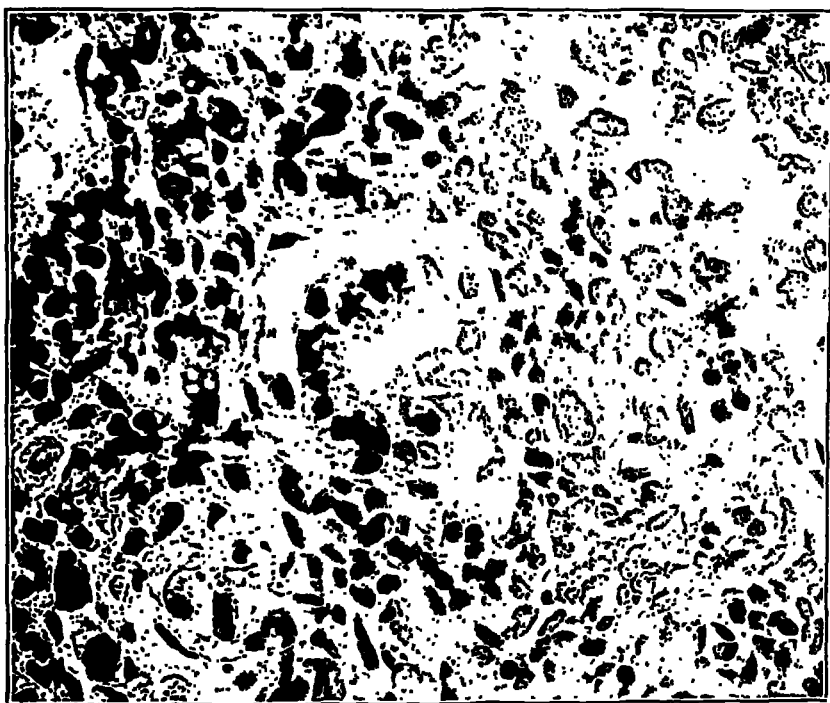


Fig. 11 (case 4).—Same section as that shown in figure 10; $\times 450$.

from observation on February 10, and was instructed to take an autogenous vaccine every five days. The rectal bleeding stopped; the weight increased from 119 to 131 pounds (54 to 59.4 Kg.), and when he returned on March 16, he felt well except for pain in the region of the tumor. On March 18, the ileocecal coil was resected, including the large tumor which the pathologist reported to be ulcerating lymphosarcoma of the cecum, without glandular involvement (figs. 12, 13 and 14). A stormy postoperative course followed; pneumonia developed and later, peritonitis. On March 21, 13 cc. of 1 per cent of mercurochrome-220 soluble was given intravenously; this was repeated two days later. The temperature, which before had remained between 103 and 104.5 F. for several days, fluctuated from 101 to 102 for the next two weeks. Following the injection of the mercurochrome, the bowels became much more active; from ten to thirteen bloody stools were passed

movements and was feeling well. Roentgen-ray treatment was again administered. He got along well, and then discontinued the vaccine early in September. On October 25, he wrote that he was having a further upset of the bowels, from nine to ten stools without blood being passed daily. A report in March, 1928, stated that he was in good condition.

COMMENT

The paucity of reports in the literature on malignant disease of the colon developing in persons with chronic ulcerative colitis is noteworthy. Struthers¹³ emphasized the relationship of chronic ulcerative colitis and polyposis, and suggested that malignant disease may follow these conditions. Hewitt and Howard¹⁴ made similar observations. Wheeler¹⁵ expresses the belief that polyposis occurs as a result of chronic ulcerative colitis. Helmholz¹⁶ called attention to the fact that Virchow and Rokitsansky may have described the terminal stage of chronic ulcerative colitis. Soper's¹⁷ work on multiple polyposis of the colon has been illuminating. At the Mayo Clinic the development of polyps has been noted proctoscopically in the course of progressing as well as healing chronic ulcerative colitis. Logan¹⁸ found polyps in 19 of 117 cases. Later, I noted 26 in 200 cases.

In view of the various reports in the literature, the frequency with which polyposis has occurred in the series of cases of chronic ulcerative colitis at the Mayo Clinic and the simultaneous occurrence of polyps and carcinoma in the diseased colon, the following hypothesis is offered: the sequence of events in some cases of malignant disease of the colon is chronic ulcerative colitis, multiple polyposis and malignant disease.

Malignant disease superimposed on chronic ulcerative colitis offers a grave prognosis. Whenever a sudden change for the worse is noted, further proctoscopic and roentgenologic investigations should be made. Operation, even if the malignant condition is discovered fairly early, yields discouraging results. One must then consider medical treatment. The only hope, it seems, is preventive treatment, that is, the cure of the colitis and the removal of the polyps.

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18. Logan, A. H.: Chronic Ulcerative Colitis: A Review of 117 Cases, *North-west Med.* 18:1, 1919.

